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Date: _____ Phone: _____ Art Unit: _____

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_____ Structure
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_____ Geninfo
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Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 13 Mar. 03 Requester's Full Name: _____ Examiner #: S. DEVI
Art Unit: 1645 Phone (308) 9347 Serial Number: 09/701,453
Results Format Preferred (circle): (PAPER) DISK E-MAIL

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

~~Title of Invention~~: DAN M. GRANOFF; HOWARD RAFF; INGEBORG S. AABERGE

Inventors (please provide full names): BJORN HANEBERG; JOHAN HOLST

Earliest Priority Date: 10-30-98

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only* Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.

Please ask MS. BEVERLY SHEARS to perform this search.

Please see attached claims with key words highlighted and/or Examples and synonyms provided.
Please include the following databases: Embase, Medline, Biosis, CA (Dialog 50), JAPIO, JICTEplus, Dialog 35, 65, 77, 144, 256, 266, 440, 348, 357, 113, 129, 130, 156 and 60.
Please perform an inventor's name search.

Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 1E05 Tel: 308-4994

Thank you. ☺

Please return the attached claims and this search request form along with the search reports.

APPENDIX B

Currently Pending Claims

1. An immunogenic composition comprising NmC oligosaccharide conjugated to a first carrier and NmB outer membrane protein.

2. The immunogenic composition of claim I wherein said first carrier is selected from the group consisting of protein, polysaccharide, polylactic acid, polyglycolic acid, polymeric amino acids, amino acid co-polymer, lipid aggregate, and inactive virus particle.

3. The immunogenic composition of claim 2 wherein said first carrier is a protein.

4. The immunogenic composition of claim 3 wherein said first carrier is CRM_{197}.

5. The immunogenic composition of claim 1 the NmB outer membrane protein is presented as proteoliposomic vesicles.

6. The immunogenic composition of claim 1 wherein said composition comprises a second carrier.

7. The immunogenic composition of claim 6 wherein said second carrier is aluminum hydroxide or MF59.

8. A method of inducing an immunologic response to NmB and NmC comprising administering an immunologically effective amount of an immunogenic composition of claim1.

Devi, S.
09/701453

-Key terms

```
     (FILE 'REGISTRY' ENTERED AT 10:19:05 ON 14 MAR 2003)
                E ALUMINUM HYDROXIDE/CN 5
L5          332 S ALUMINUM HYDROXIDE?/CN
                E MF59/CN 5
                E MF 59/CN 5
L6            1 S E3
                E ALUM/CN 5
L7            2 S E3
                E ALHYDROGEL/CN 5
L8            1 S E3
L9          335 S L5 OR L6 OR L7 OR L8

     FILE 'HCAPLUS' ENTERED AT 10:20:28 ON 14 MAR 2003
L1         2021 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NMC OR MENC OR (NM OR
                MEN OR MENINGOCOCC## OR MENINGITID?)(S)((GROUP OR
                SEROGROUP)(W)C)
L2         1079 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NMB OR MENB OR (NM OR
                MEN OR MENINGOCOCC## OR MENINGITID?)(S)((GROUP OR
                SEROGROUP)(W)B)
L3          131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L2
L5          332 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALUMINUM HYDROXIDE?/CN

L6            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "MF 59"/CN
L7            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALUM/CN
L8            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALHYDROGEL/CN
L9          335 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 OR L6 OR L7 OR L8
L15          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND (L9 OR ALUM OR
                (AL OR ALUMIN?)(W)(OH OR HYDROXIDE) OR ALOH# OR ALHYDROGE
                L OR ALHYDRO GEL OR MF59 OR MF 59)

L15  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:76644  HCAPLUS
DOCUMENT NUMBER:          138:121627
TITLE:                    Purification of bacterial capsular
                          polysaccharide for use in combination vaccines
INVENTOR(S):              Costantino, Paolo
PATENT ASSIGNEE(S):       Chiron S.P.A., Italy
SOURCE:                   PCT Int. Appl., 49 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2003007985      A2   20030130      WO 2002-IB3191   20020620
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
             SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
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WO 2003009869 A1 20030206 WO 2002-IB3495 20020726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 2001-15176 A 20010620
GB 2001-18249 A 20010726
WO 2002-IB3191 W 20020620

AB The invention provides a process for purifying a bacterial capsular polysaccharide, comprising the steps of (a) pptn. of said polysaccharide, followed by (b) solubilization of the pptd. polysaccharide using ethanol. CTAB can be used for step (a). The material obtained, preferably following hydrolysis and sizing, can be conjugated to a carrier protein and formulated as a vaccine. Also, in vaccines comprising saccharides from the serogroups A and C, the invention provides that the ratio (wt./wt.) of MenA saccharide : **MenC** saccharide is >1.

IT **21645-51-2, Aluminum hydroxide,**
biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(purifn. of Neisseria meningitidis capsular polysaccharide for use in combination vaccines)

L15 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:545516 HCAPLUS
DOCUMENT NUMBER: 135:136409
TITLE: Outer membrane vesicle (OMV) vaccine comprising N. **meningitidis serogroup B** outer membrane proteins
INVENTOR(S): Pizza, Mariagrazia; Rappuoli, Rino; Giuliani, Marzia
PATENT ASSIGNEE(S): Chiron S.p.A., Italy
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052885	A1	20010726	WO 2001-IB166	20010117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1248647 A1 20021016 EP 2001-942562 20010117

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: GB 2000-1067 A 20000117
GB 2000-5699 A 20000309
WO 2001-IB166 W 20010117

AB A compn. comprising (a) Neisseria **meningitidis serogroup B** outer membrane vesicles (OMVs), and (b) an immunogenic component selected from other Neisseria proteins, or immunogenic fragments thereof. Component (b) preferably includes a protein from a different **NmB** strain from that from which the OMV of component (a) is derived. The OMVs are preferably obtained by deoxycholate extn. Optionally, the compn. may also comprise a protective antigen against other pathogens.

IT **21645-51-2, Aluminum hydroxide,**
biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine compns. comprising Neisseria **meningitidis group B** outer membrane vesicles)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:396693 HCAPLUS
DOCUMENT NUMBER: 135:32728
TITLE: Compositions comprising Neisseria meningitidis antigens from serogroups B and C
INVENTOR(S): Giuliani, Marzia Monica; Pizza, Mariagrazia; Rappuoli, Rino
PATENT ASSIGNEE(S): Chiron Spa, Italy
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037863	A2	20010531	WO 2000-IB1940	20001129
WO 2001037863	A3	20011227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1235589 A2 20020904 EP 2000-981554 20001129

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: GB 1999-28196 A 19991129
WO 2000-IB1940 W 20001129

AB International patent application WO99/61053 discloses immunogenic compns. that comprise N. meningitidis serogroup C oligosaccharide conjugated to a carrier, in combination with N. meningitidis serogroup B outer membrane protein. These are disclosed in the present application in combination with further Neisserial proteins and/or protective antigens against other pathogenic organisms (e.g. Haemophilus influenzae, DTP, HBV, etc.).

L15 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:144761 HCAPLUS
DOCUMENT NUMBER: 132:193251
TITLE: Immunogenic .beta.-propionamido-linked polysaccharide protein conjugate useful as a vaccine produced using an N-acryloylated polysaccharide
INVENTOR(S): Michon, Francis; Huang, Chun-Hsien; Uitz, Catherine
PATENT ASSIGNEE(S): North American Vaccine, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010599	A2	20000302	WO 1999-US18982	19990818
WO 2000010599	A3	20000622		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2340692	AA	20000302	CA 1999-2340692	19990818
AU 9957800	A1	20000314	AU 1999-57800	19990818
EP 1109576	A2	20010627	EP 1999-945115	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
NO 2001000805	A	20010403	NO 2001-805	20010216

PRIORITY APPLN. INFO.: US 1998-97120P P 19980819
US 1999-376911 A 19990818
WO 1999-US18982 W 19990818

AB Novel immunogenic .beta.-propionamido-linked polysaccharide- and N-propionamido-linked oligosaccharide-protein conjugates are provided as well as method of producing the conjugates. The conjugation procedure is simple, rapid, reproducible and applicable to a variety of polysaccharides or oligosaccharides derived from bacterial species, yeast, cancer cells or chem. synthesized. Vaccines and methods of immunization against infection or cancer using the immunogenic .beta.-propionamido-linked polysaccharide- and

.beta.-propionamido-linked oligosaccharide-protein conjugates are also disclosed.

L15 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:763897 HCAPLUS
DOCUMENT NUMBER: 132:15578
TITLE: Combination meningitidis B/C vaccines
INVENTOR(S): Granoff, Dan M.; Aaberge, Ingeborg S.; Haneberg, Bjorn; Holst, Johan; Raff, Howard
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961053	A1	19991202	WO 1999-US11977	19990528
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2332963	AA	19991202	CA 1999-2332963	19990528
AU 9942215	A1	19991213	AU 1999-42215	19990528
BR 9910749	A	20010213	BR 1999-10749	19990528
EP 1079857	A1	20010307	EP 1999-926046	19990528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002516292	T2	20020604	JP 2000-550512	19990528

PRIORITY APPLN. INFO.:
US 1998-87351P P 19980529
US 1998-106446P P 19981030
WO 1999-US11977 W 19990528

AB A combination vaccine for Neisseria **meningitidis** (**Nm**) comprising outer membrane proteins from **serogroup B** and oligosaccharides from **serogroup C**, and its use for the prevention or treatment of disease is disclosed. Pigs were injected with two injection of **NmC** conjugate/**NmB**/**MF59** (10.mu.g/25.mu.g/0.5 mL) sepd. by 28 days. The combination vaccine immunogenic as measured by **NmB** and **NmC** IgG antibody titers, resp. The antibody response induced by the combination vaccine was significantly greater than the antibody response induced by either the **NmC** conjugate alone, or the combination of **NmC** conjugate and **NmB** in the presence of **alum**. When adjuvant **MF59** was present, the antibody titer for the combination vaccine increased approx. six-fold.

IT **21645-51-2**, **Aluminum hydroxide** (**Al**(**OH**)3), biological studies **172889-84-8** , **Mf59**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination meningitidis B/C vaccines)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:340244 HCAPLUS
DOCUMENT NUMBER: 129:121375
TITLE: Effect of **aluminum hydroxide** and **meningococcal serogroup C** capsular polysaccharide on the immunogenicity and reactogenicity of a **group B** Neisseria **meningitidis** outer membrane vesicle vaccine
AUTHOR(S): Rosenqvist, E.; Hoiby, E. A.; Bjune, G.; Aase, A.; Halstensen, A.; Lehmann, A. K.; Paulssen, J.; Holst, J.; Michaelsen, T. E.; Nokleby, H.; Froholm, L. O.; Closs, O.
CORPORATE SOURCE: Departments of Vaccinology and Bacteriology, National Institute of Public Health, Oslo, Norway
SOURCE: Developments in Biological Standardization (1998), 92(Modulation of the Immune Response to Vaccine Antigens), 323-333
CODEN: DVBSA3; ISSN: 0301-5149
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three different formulations of an outer membrane vesicle (OMV) vaccine against **group B meningococcal** disease have been prepd. and tested for immunogenicity and reactogenicity in adult volunteers. The vaccines were prepd. with or without **aluminum hydroxide** and serogroup C-polysaccharide (C-ps). Doses from 12.5 to 100 .mu.g protein were given twice at a six weeks' interval. All three formulations were well tolerated and highly immunogenic, inducing bactericidal and opsonizing antibodies in humans. Adsorption of OMVs to **aluminum hydroxide** reduced the pyrogenicity in rabbits. The differences in immunogenicity between the formulations were relatively small, but after the second dose a stronger booster response was obsd. when the vaccines were adsorbed. Thus, a formulation with OMVs and C-ps represents a safe and highly immunogenic vaccine, even without **aluminum hydroxide**.
IT **21645-51-2, Aluminum hydroxide,** biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**aluminum hydroxide** and **meningococcal serogroup C** capsular polysaccharide effect on immunogenicity and reactogenicity of **group B** Neisseria **meningitidis** outer membrane vesicle vaccine)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:97206 HCAPLUS
DOCUMENT NUMBER: 128:203874
TITLE: Meningococcal vaccine development: a novel approach
AUTHOR(S): Fusco, Peter C.; Blake, M. S.; Michon, Francis
CORPORATE SOURCE: North American Vaccine, Inc., Beltsville, MD, 20705, USA
SOURCE: Expert Opinion on Investigational Drugs (1998), 7(2), 245-252
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neisseria meningitidis is a major world-wide cause of meningitis. Effective capsular polysaccharide (CPS) vaccines, that elicit CPS-specific bactericidal (BC) antibodies, were previously developed and licensed to protect against meningococcal disease. However, due to their T-cell independent character, CPS vaccines are useless in infants and do not provide immunol. memory or long-lasting protection in adults. CPS-protein conjugate vaccines are being developed to improve and broaden vaccine efficacy by creating T-cell dependent antigens. However, **group B meningococci** (GBM) are responsible for nearly half of **meningococcal** disease and possess a CPS, composed of polysialic acid, that is poorly immunogenic. N-propionyl (NPr) modification of the GBM polysaccharide (GBMP) has enhanced its immunogenicity, but BC antibodies are not induced at high levels, even when conjugated to conventional protein carriers, unless adjuvants stronger than **aluminum hydroxide** are used. We have chosen to couple the NPr-GBMP by reductive amination to a recombinant GBM class 3 porin (rProB), which we have shown to modulate the immune response in animals towards the prodn. of CPS-specific BC antibodies. We have also combined this conjugate with similar CPS-rProB conjugates for groups A and C meningococci to form a trivalent A/B/C conjugate vaccine. This trivalent meningococcal vaccine has been shown to be safe and highly immunogenic in mice and non human primates, generating CPS-specific BC antibodies for each of the 3 major serogroups, which should provide world-wide protection against meningococcal disease.

L15 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:58677 HCAPLUS
DOCUMENT NUMBER: 124:114852
TITLE: Antibody studies in mice of outer membrane antigens for use in an improved meningococcal B and C vaccine
AUTHOR(S): Milagres, Lucimar G.; Brandileone, Maria Cristina C.; Sacchi, Claudio T.; Vieira, Vera S. D.; Zanella, Rosemeire C.; Frasch, Carl E.
CORPORATE SOURCE: Bacteriology Branch, Adolfo Lutz Institute, Av. Dr. Arnaldo, 351, Cerqueira Cesar, CEP 01246 902, Sao Paulo, SP, Brazil
SOURCE: FEMS Immunology and Medical Microbiology (1996), 13(1), 9-17
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Since 1988, N. meningitidis, B:4:P1.15, ET-5 complex, has been responsible for an epidemic of meningococcal disease in Greater Sao Paulo, Brazil. Despite current trials to develop an effective vaccine against **group B meningococci**, children less than 2 yr old have not been protected. It has been suggested that iron-regulated proteins (IRPs) should be considered as potential antigens for meningococcal vaccines. The vaccines under study consisted of outer-membrane vesicles depleted of lipooligosaccharide from three **serogroup B** strains and one **serogroup C** strain, IRPs, **meningococcal group C** polysaccharide and **aluminum hydroxide**. Four different protein and C polysaccharide concns. were studied. The ELISA and bactericidal results showed a higher antibody response when 2 injections of 2.0 .mu.g doses were administered. Despite higher IgG reactivity against antigen prepns. contg. IRPs seen in ELISA, the bactericidal activity was not increased if the target strain was grown in iron-restricted medium. The influence of addn. of alk.-detoxified lipooligosaccharide (dLOS) on immunogenicity of the vaccine was also investigated, and the dLOS provided for a more functionally specific antibody response.

L15 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:480195 HCAPLUS
DOCUMENT NUMBER: 119:80195
TITLE: Protein-dimeric polysaccharide conjugate vaccine
INVENTOR(S): Marburg, Stephen; Tolman, Richard L.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 534764	A1	19930331	EP 1992-308730	19920924
R: CH, DE, FR, GB, IT, LI, NL				
US 5371197	A	19941206	US 1991-766242	19910924
CA 2078359	AA	19930325	CA 1992-2078359	19920916
JP 05279399	A2	19931026	JP 1992-254695	19920924

PRIORITY APPLN. INFO.: US 1991-766242 19910924

AB A conjugate immunogen having polysaccharide moieties derived from bacterial sources, provides a multivalent vaccine with a low protein to polysaccharide ratio. The vaccine reduces complications assocd. with injection of protein immunogens due to pyrogenic responses, such as swelling and pain, and is particularly suitable for administration to infants. OmpC protein conjugates with polyribosyl-ribitol-phosphate (PRP) was reacted with Streptococcus pneumoniae 6A polysaccharide (PnPs6A) to obtain a gelatinous mixt., which was filtered and washed. PnPs6A-PRP-OmpC conjugate was adsorbed onto **Al(OH)**3, then was i.m. administered to chinchillas at the dose of 0.08.mu.g PnPs6A and 0.12.mu.g PRP at 0 and 4 wks and animals were bled at 0, 2, 4, 6, and 8 wks. There were high titers of both anti-PnPs6A and anti-PRP antibody.

L15 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:4250 HCAPLUS
DOCUMENT NUMBER: 102:4250
TITLE: Development of a Neisseria **meningitidis** **group B** serotype 2b protein vaccine and evaluation in a mouse model
AUTHOR(S): Wang, Li Ya; Frasch, Carl E.
CORPORATE SOURCE: Off. Biol., Cent. Drugs Biol., Bethesda, MD, 20205, USA
SOURCE: Infection and Immunity (1984), 46(2), 408-14
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although serotype 2 remains the predominant cause of **group B** N. **meningitidis** disease in many parts of the world, most cases of this disease are now due to serotype 2b rather than 2a. For this reason, the serotype 2a vaccine method of C. E. Frasch and M. S. Peppler (1982) was adapted to the prodn. of a serotype 2b protein vaccine. A spontaneously occurring nonencapsulated mutant of the group B serotype 2b strain 3006 was obtained by selection on group B antiserum agar. Serotype 2b outer membrane protein vaccines were prepd. with less than 1% lipopolysaccharide contamination. The immunogenicity of these vaccines was evaluated in mice in the presence and absence of **meningococcal group B** and **group C** capsular polysaccharides. The group B and C polysaccharides equally potentiated the antibody response to the serotype 2b protein. Addn. of **aluminum hydroxide** or aluminum phosphate markedly improved the antibody response to the serotype 2b protein, but **aluminum hydroxide** -adjuvanted vaccines consistently elicited higher antibody levels. **Aluminum hydroxide**-adsorbed serotype 2a and 2b protein vaccines were evaluated for induction of cross-protective bactericidal antibodies. The 2a vaccines were 2a specific, whereas the 2b vaccines elicited antibodies strongly bactericidal for both 2a and 2b meningococcal strains and protected against bacteremia in a mouse model. It may therefore be possible to provide protection against both 2a and 2b disease by using an **aluminum hydroxide**-adsorbed protein vaccine contg. a single serotype 2 protein component.
IT **21645-51-2**, biological studies
RL: BIOL (Biological study)
(as immune adjuvant, antibody response to Neisseria **meningitidis group B** serotype 2b protein vaccine response to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:30:04 ON 14 MAR 2003)
L18 23 S L15
L19 13 DUP REM L18 (10 DUPLICATES REMOVED)

L19 ANSWER 1 OF 13 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1
ACCESSION NUMBER: 2001-367614 [38] WPIDS
DOC. NO. CPI: C2001-112781
TITLE: Immunogenic composition for treating Neisserial bacteria infection, has Neisseria **meningitidis** antigens from **serogroups B**, C with further

Neisserial proteins and protective antigens against other pathogenic organisms.

DERWENT CLASS: B04 D16
INVENTOR(S): GIULIANI, M M; PIZZA, M; RAPPUOLI, R
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001037863	A2	20010531	(200138)*	EN	27

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001018785	A		20010604	(200153)	
EP 1235589	A2		20020904	(200266)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001037863	A2	WO 2000-IB1940	20001129
AU 2001018785	A	AU 2001-18785	20001129
EP 1235589	A2	EP 2000-981554	20001129
		WO 2000-IB1940	20001129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001018785	A	Based on	WO 200137863
EP 1235589	A2	Based on	WO 200137863

PRIORITY APPLN. INFO: GB 1999-28196 19991129
AN 2001-367614 [38] WPIDS
AB WO 200137863 A UPAB: 20010711

NOVELTY - An immunogenic composition (I) comprising Neisseria **meningitidis** (**Nm**) **serogroup C** oligosaccharide and **Nm serogroup B** outer membrane protein, in combination with proteins (P1) (or its immunogenic fragments) and/or protective antigens against **Nm** serogroups A, W or Y, Hemophilus influenza, Pneumococcus, diphtheria, tetanus, whooping cough, hepatitis B virus and/or Helicobacter pylori, is new.

DETAILED DESCRIPTION - An immunogenic composition (I) comprising Neisseria **meningitidis** (**Nm**) **serogroup C** oligosaccharide and **Nm serogroup B** outer membrane protein, in combination with proteins (P1) (or its immunogenic fragments) and/or protective antigens against **Nm** serogroups A, W or Y, Hemophilus influenza, Pneumococcus, diphtheria, tetanus, whooping cough, hepatitis B virus and/or Helicobacter pylori, is new.

P1, or its immunogenic fragments, is disclosed in WO99/57280, WO99/36544, WO99/24578, WO97/28273, WO96/29412, WO95/03413 or WO99/31132.

INDEPENDENT CLAIMS are also included for the following:

(1) an immunogenic composition comprising **NmC** oligosaccharide and **NmB** proteins 919, 287 and/or ORF1; and

(2) a vaccine comprising (I).

ACTIVITY - Antibiotic.

MECHANISM OF ACTION - Vaccine.

Groups of guinea pigs received one of **NmC** conj./**alum**, **NmB**/**alum**, **NmC** conj./**NmB**/**alum** and **NmC** conj./**NmB**/**MF59** vaccine components. Each animal received two injections, intramuscularly (IM), separated by 28 days. Serum samples were obtained prior to each injection and 18 days after the second injection. Each dose consisted of two 0.25 ml IM injections. Serum samples were assayed for IgG anticapsular antibody concentrations to **NmC** and for IgG anti-outer membrane vesicle antibody concentrations to **NmB** by ELISA. A specific anti-meningococcal B antibody response was induced by the vaccine combinations comprising **NmB** and a specific anti-meningococcal C antibody response was induced by the vaccine combinations comprising **NmC**. The antibody response induced by the combination of **NmC** conjugate and **NmB** in the presence of **MF59** adjuvant was significantly greater than the antibody response induced by either the **NmC** conjugate alone or the combination of the **NmC** conjugate and **NmB** in the presence of **alum**. When the adjuvant **MF59** was present, the antibody titer for the combination vaccine increased approximately 6-fold. Serum samples were also tested for complement-mediated bactericidal titers to **MenC** strain 60E and **MenB** strain 44/76. The combination vaccine elicited high titers of serum bactericidal antibody for both **NmB** and **NmC**. 2-5 fold higher **NmB** bactericidal titers were obtained with the combination vaccine than with the **NmB** vaccine alone. The antibodies directed to meningococcal B and C induced by the vaccine combinations comprising **NmB** and **NmC** were bactericidal.

USE - (I) is useful for treating or preventing infection due to Neisserial bacteria.

Dwg.0/2

L19 ANSWER 2 OF 13 MEDLINE

ACCESSION NUMBER: 2001406624 MEDLINE
DOCUMENT NUMBER: 21351499 PubMed ID: 11457545
TITLE: Modulation of the serological response to meningococcal polysaccharides by cytokines.
AUTHOR: Cortes-Castillo M A; Thorpe R; Corbel M J
CORPORATE SOURCE: Division of Bacteriology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, EN6 3QG, Hertfordshire, UK.
SOURCE: VACCINE, (2001 Jul 20) 19 (30) 4194-203. Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20011001
Last Updated on STN: 20011001
Entered Medline: 20010927

AB Meningococcal A and C but not B capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with **aluminium hydroxide** and outer membrane proteins. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/+) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

L19 ANSWER 3 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:395040 BIOSIS
DOCUMENT NUMBER: PREV200000395040
TITLE: Preclinical studies on a novel trivalent **meningococcal** conjugate vaccine for **serogroups B**, C, and Y.
AUTHOR(S): Fusco, P. C. (1); Farley, E. K. (1); Huang, C. H. (1); Blake, M. S. (1); Michon, F. (1)
CORPORATE SOURCE: (1) North American Vaccine, Inc., Columbia, MD USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 304. print.
Meeting Info.: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L19 ANSWER 4 OF 13 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-097070 [08] WPIDS
DOC. NO. CPI: C2000-028122
TITLE: Immunogenic composition for the prevention and treatment of diseases caused by **serogroups B** and C strains of Neisseria **meningitidis**.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): AABERGE, I S; GRANOFF, D M; HANEBERG, B; HOLST, J; RAFF, H
PATENT ASSIGNEE(S): (CHIR) CHIRON CORP
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9961053	A1	19991202	(200008)*	EN	24
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9942215	A	19991213	(200020)		
BR 9910749	A	20010213	(200114)		
EP 1079857	A1	20010307	(200114)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002516292	W	20020604	(200239)		25

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9961053	A1	WO 1999-US11977	19990528
AU 9942215	A	AU 1999-42215	19990528
BR 9910749	A	BR 1999-10749	19990528
		WO 1999-US11977	19990528
EP 1079857	A1	EP 1999-926046	19990528
		WO 1999-US11977	19990528
JP 2002516292	W	WO 1999-US11977	19990528
		JP 2000-550512	19990528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9942215	A	Based on	WO 9961053
BR 9910749	A	Based on	WO 9961053
EP 1079857	A1	Based on	WO 9961053
JP 2002516292	W	Based on	WO 9961053

PRIORITY APPLN. INFO: US 1998-106446P 19981030; US 1998-87351P 19980529

AN 2000-097070 [08] WPIDS

AB WO 9961053 A UPAB: 20000215

NOVELTY - An immunogenic composition (I) comprising Neisseria **meningitidis serogroup C** (**NmC**) oligosaccharide conjugated to a first carrier and Neisseria **meningitidis serogroup B** (**NmB**) outer membrane protein, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of inducing an immunologic response to **NmB** and **NmC** comprising administering (I);

(2) a vaccine comprising (I); and

(3) a method of vaccinating an individual comprising administering (I).

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - The immunogenic composition is used for the prevention or treatment of diseases caused by **serogroups B** and

C strains of Neisseria **meningitidis**.
ADVANTAGE - The composition can induce immune response to both **serogroups B** and C strains of Neisseria **meningitidis**.
Dwg.0/4

L19 ANSWER 5 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:281611 BIOSIS
DOCUMENT NUMBER: PREV199800281611
TITLE: Effect of **aluminium hydroxide** and **meningococcal serogroup C** capsular polysaccharide on the immunogenicity and reactogenicity of a **group B** Neisseria **meningitidis** outer membrane vesicle vaccine.
AUTHOR(S): Rosenqvist, E. (1); Hoiby, E. A.; Bjune, G.; Aase, A.; Halstensen, A.; Lehmann, A. K.; Paulssen, J.; Holst, J.; Michaelsen, T. E.; Nokleby, H.; Froholm, L. O.; Closs, O.
CORPORATE SOURCE: (1) Dep. Vaccinol., Natl. Inst. Public Health, P.O. Box 4404 Torshov, N-0403 Oslo Norway
SOURCE: Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 323-333. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens.
Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization
. ISSN: 0301-5149. ISBN: 3-8055-6640-9.
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L19 ANSWER 6 OF 13 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998214909 MEDLINE
DOCUMENT NUMBER: 98214909 PubMed ID: 9554288
TITLE: Effect of **aluminium hydroxide** and **meningococcal serogroup C** capsular polysaccharide on the immunogenicity and reactogenicity of a **group B** Neisseria **meningitidis** outer membrane vesicle vaccine.
AUTHOR: Rosenqvist E; Hoiby E A; Bjune G; Aase A; Halstensen A; Lehmann A K; Paulssen J; Holst J; Michaelsen T E; Nokleby H; Froholm L O; Closs O
CORPORATE SOURCE: Department of Vaccinology, National Institute of Public Health, Oslo, Norway.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 323-33.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Three different formulations of an outer membrane vesicle (OMV) vaccine against **group B meningococcal** disease have been prepared and tested for immunogenicity and reactogenicity in adult volunteers. The vaccines were prepared with or without **aluminium hydroxide** and **serogroup C**-polysaccharide (C-ps). Doses from 12.5 to 100 micrograms protein were given twice at a six weeks' interval. All three formulations were well tolerated and highly immunogenic, inducing bactericidal and opsonizing antibodies in humans. Adsorption of OMVs to **aluminium hydroxide** reduced the pyrogenicity in rabbits. The differences in immunogenicity between the formulations were relatively small, but after the second dose a stronger booster response was observed when the vaccines were adsorbed. Thus, a formulation with OMVs and C-ps represents a safe and highly immunogenic vaccine, even without **aluminium hydroxide**.

L19 ANSWER 7 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96418608 MEDLINE
DOCUMENT NUMBER: 96418608 PubMed ID: 8821393
TITLE: Antibody studies in mice of outer membrane antigens for use in an improved meningococcal B and C vaccine.
AUTHOR: Milagres L G; Cristina M; Brandileone M C; Sacchi C T; Vieira V S; Zanella R C; Frasch C E
CORPORATE SOURCE: Bacteriology Branch, Adolfo Lutz Institute, Sao Paulo, Brazil.
SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (1996 Jan) 13 (1) 9-17.
Journal code: 9315554. ISSN: 0928-8244.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961126

AB Since 1988, N. **meningitidis**, B:4:P1.15, ET-5 complex, has been responsible for an epidemic of **meningococcal** disease in Greater Sao Paulo, Brazil. Despite current trials to develop an effective vaccine against **group B meningococci**, children less than 2 years old have not been protected. It has been suggested that iron-regulated proteins (IRPs) should be considered as potential antigens for **meningococcal** vaccines. The vaccines under study consisted of outer-membrane vesicles depleted of lipooligosaccharide from three **serogroup B** strains and one **serogroup C** strain, IRPs, **meningococcal group C** polysaccharide and **aluminum hydroxide**. Four different protein and C polysaccharide concentrations were studied. The ELISA and bactericidal results showed a higher antibody response when 2 injections of 2.0 micrograms doses were administered. Despite higher IgG reactivity against antigen

preparations containing IRPs seen in ELISA, the bactericidal activity was not increased if the target strain was grown in iron-restricted medium. The influence of addition of alkaline-detoxified lipooligosaccharide (dLOS) on immunogenicity of the vaccine was also investigated, and the dLOS provided for a more functionally specific antibody response.

L19 ANSWER 8 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91315786 MEDLINE
DOCUMENT NUMBER: 91315786 PubMed ID: 1907153
TITLE: Immunization against **serogroup B meningococci**. Opsonin response in vaccinees as measured by chemiluminescence.
AUTHOR: Lehmann A K; Halstensen A; Naess A; Vollset S E; Sjursen H; Bjune G
CORPORATE SOURCE: Medical Department B, University of Bergen, Norway.
SOURCE: APMIS, (1991 Aug) 99 (8) 769-72.
Journal code: 8803400. ISSN: 0903-4641.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910922
Last Updated on STN: 19970203
Entered Medline: 19910830

AB One hundred and thirteen healthy volunteers were immunized twice (six weeks apart) with four different doses (12.5, 25, 50 and 100 micrograms, measured as protein content) of an outer membrane vesicle vaccine from a **serogroup B meningococcal** strain (44/76, B:15:P1.16) complexed to **serogroup C meningococcal** polysaccharide and/or **Al(OH)**3 i.e. 12 different vaccines. Serum opsonic activity against the **serogroup B** strain was measured using a chemiluminescence method. A significant rise in serum opsonic activity was demonstrated in 84 volunteers (74%) six weeks after the first injection and in 97 (86%) six weeks after the second. All vaccinees with low preimmunization values (less than 25 mVs) experienced a significant increase in opsonic activity. A dose-related response was most evident for the vaccines containing adjuvant, and these vaccines were associated with a maximum response six weeks after the second injection, while the vaccines without **Al(OH)**3 induced a peak response six weeks after the first injection. The postimmunization opsonic activity was similar to that found in convalescent sera, indicating that the vaccines may protect against **serogroup B meningococcal** disease.

L19 ANSWER 9 OF 13 MEDLINE
ACCESSION NUMBER: 92253082 MEDLINE
DOCUMENT NUMBER: 92253082 PubMed ID: 1687481
TITLE: Human antibody responses after vaccination with the Norwegian **group B meningococcal** outer membrane vesicle vaccine: results from ELISA studies.
AUTHOR: Rosenqvist E; Hoiby E A; Bjune G; Bryn K; Closs O; Feiring B; Klem A; Nokleby H; Frolm L O
CORPORATE SOURCE: Department of Vaccine, National Institute of Public

Health, Oslo.
SOURCE: NIPH ANNALS, (1991 Dec) 14 (2) 169-79; discussion 180-1.
Journal code: 7805819. ISSN: 0332-5652.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19950206
Entered Medline: 19920610

AB Antibody responses after vaccination with three different formulations of a new **meningococcal group B** outer membrane vesicle (OMV) vaccine have been studied with the ELISA technique using four different antigens. Sera from about 1200 vaccinees participating in steps 1, 2, 3 and 6 of the phase II clinical trials in Norway were analysed. The effects of non-covalently complexing the OMV antigen to **group C** polysaccharide (C-PS) and of adsorbing OMV (with and without C-PS) to **aluminium hydroxide** (AH) were studied. All three vaccine formulations were highly immunogenic in humans. Adsorption of the vaccine to AH had a relatively small effect on the immune response, but the results indicated that the booster response was stronger with the adsorbed than with the unadsorbed vaccines. Some increase in the immune response against OMV was also observed by non-covalent complexing OMV with C-PS, particularly after the second dose. In most of the vaccinees the antibody levels were significantly reduced 6 to 12 months after vaccination. Adsorption of the vaccine to AH had no effect on the antibody response against C-PS. Comparison with bactericidal activity of the same sera was done. A highly significant correlation was observed between the bactericidal titres and the levels of IgG antibodies against OMV and class 5C protein, whereas the correlation between antibody levels against lipopolysaccharide and the bactericidal activity was poor.

L19 ANSWER 10 OF 13 MEDLINE
ACCESSION NUMBER: 92253081 MEDLINE
DOCUMENT NUMBER: 92253081 PubMed ID: 1812430
TITLE: Serum opsonins to **serogroup B meningococci** after disease and vaccination.
AUTHOR: Halstensen A; Lehmann A K; Guttormsen H K; Vollset S E; Bjune G; Naess A
CORPORATE SOURCE: Medical Department B, University of Bergen, Haukeland Hospital.
SOURCE: NIPH ANNALS, (1991 Dec) 14 (2) 157-65; discussion 166-7.
Journal code: 7805819. ISSN: 0332-5652.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19920619
Entered Medline: 19920610

AB In this review the results of three previous studies are compared

and discussed. Sera from 101 patients with **meningococcal** disease and from 113 volunteers immunized twice with vaccine preparations against **serogroup B** **meningococci** were examined for antimeningococcal opsonic activity using a chemiluminescence (CL) method. Twelve groups of vaccinees were immunized twice with one of four different doses of an outer membrane vesicle (OMV) preparation either alone or complexed to **serogroup C** polysaccharide and/or the adjuvant **Al(OH)**3. The OMV vaccine strain (44/76) was a patient isolate characterized as B:15:P1.16. The 89 surviving patients and 97/113 volunteers responded with significantly increased opsonic activity to the vaccine strain. Sera from all vaccinees with low preimmunization levels demonstrated a significant postimmunization increase in opsonic activity. The vaccine response was dose related, and the second injection induced a booster response in those who received preparations containing **Al(OH)**3. At 26 weeks a reduction in opsonic activity to preimmunization levels was noted in 19/97 previous responders. The reduction was less pronounced in those who were immunized with the higher doses. Using CL and flow cytometry we found vaccinee sera to show cross reacting opsonin responses to other serogroups and serotypes of **meningococci** except **meningococci** of serotype 2a and 2b. The increase in antimeningococcal opsonins after vaccination suggests that the **serogroup B** OMV vaccine may induce protection against clinical disease.

L19 ANSWER 11 OF 13 MEDLINE

ACCESSION NUMBER:	88221117 MEDLINE
DOCUMENT NUMBER:	88221117 PubMed ID: 3130778
TITLE:	Appearance of new strains associated with **group B meningococcal** disease and their use for rapid vaccine development.
AUTHOR:	Frasch C E; Mocca L F; Karpas A B
CORPORATE SOURCE:	Office of Biologics, Food and Drug Administration, Bethesda, MD 20892.
SOURCE:	ANTONIE VAN LEEUWENHOEK, (1987) 53 (6) 395-402. Journal code: 0372625. ISSN: 0003-6072.
PUB. COUNTRY:	Netherlands
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	198806
ENTRY DATE:	Entered STN: 19900308 Last Updated on STN: 19900308 Entered Medline: 19880623

AB There has been a decrease in the prevalence of disease in the United States due to **meningococcal** serotypes 2a and 2b containing class 2 proteins with a concomitant increase in nonserotypable strains containing class 3 major outer membrane proteins. A new disease associated strain was identified using monoclonal antibodies as B:4:P1.15. Serotype 4 strains have been heretofore isolated almost only from carriers. This B:4:P1.15 strain predominated among **group B** disease isolates in Cuba from the late 1970s to the present and among Miami, Florida isolates recovered in 1981 and 1982. To determine whether protein vaccines for new strains or serotypes could be prepared using our present methods, a combined vaccine was prepared from a **group B** strain

(B:8:P1.15) recovered during a recent outbreak in Virginia, and a serotype 2b strain, plus **group C** polysaccharide. The vaccine was prepared with **aluminum hydroxide**, or with trehalose dimycolate plus monophosphoryl lipid A, or without adjuvant. Four weeks after immunization antibody levels were much higher in mice that received vaccine containing adjuvant.

L19 ANSWER 12 OF 13 MEDLINE
ACCESSION NUMBER: 86299908 MEDLINE
DOCUMENT NUMBER: 86299908 PubMed ID: 3743232
TITLE: Sources and speciation of aluminium and silicon in natural waters.
AUTHOR: Farmer V C
SOURCE: CIBA FOUNDATION SYMPOSIUM, (1986) 121 4-23. Journal code: 0356636. ISSN: 0300-5208.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19861023

AB The aluminosilicate minerals of igneous and metamorphic rocks are mostly unstable in earth-surface weathering conditions. In the tropics and subtropics, they are transformed to stable end-products (crystalline clay minerals, oxides and hydroxides) that largely conserve aluminium and iron. In noncalcareous soils in temperature and boreal climates, aluminium can be markedly mobile, and is precipitated as metastable products that include hydrous aluminosilicates, hydroxyaluminium polymers in or on 2:1 layer silicates, and complexes with soil organic matter. The aluminosilicate precipitates formed at pH less than 5.5 have structures related to imogolite, a unidimensional crystal in the form of a tube of 2.3 **nm** outer diameter. These metastable precipitates, both organic and inorganic, are readily remobilized on further acidification, and can release aluminium into streams if the solutions are not neutralized in the subsoil. Three classes of soluble aluminium species in natural waters have been distinguished by their rate of reaction with complexing reagents, and their rate of adsorption on cation-exchange columns. These are: (a) unreactive, acid-soluble, Al, (b) labile monomeric Al, and (c) non-liable monomeric Al. **Group** (**b**) includes simple inorganic species (e.g. Al3+, **AlOH2**+, AlF2+), and **group** (**c**) is thought to include organic complexes. In contrast, silicon occurs dominantly as Si(OH)4 monomers in natural water. Its metastable precipitates include hydrous aluminosilicates and biogenic opal.

L19 ANSWER 13 OF 13 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 85053438 MEDLINE
DOCUMENT NUMBER: 85053438 PubMed ID: 6437983
TITLE: Development of a Neisseria **meningitidis** **group B** serotype 2b protein vaccine and evaluation in a mouse model.
AUTHOR: Wang L Y; Frasch C E
SOURCE: INFECTION AND IMMUNITY, (1984 Nov) 46 (2) 408-14. Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198412
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19841224

AB Although serotype 2 remains the predominant cause of **group B** Neisseria **meningitidis** disease in many parts of the world, most cases of this disease are now due to serotype 2b rather than 2a. For this reason, we adapted the serotype 2a vaccine method of C. E. Frasch and M. S. Peppler (Infect. Immun. 37:271-280, 1982) to the production of a serotype 2b protein vaccine. A spontaneously occurring nonencapsulated mutant of the **group B** serotype 2b strain 3006 was obtained by selection on **group B** antiserum agar. Serotype 2b outer membrane protein vaccines were prepared with less than 1% lipoplysaccharide contamination. The immunogenicity of these vaccines was evaluated in mice in the presence and absence of **meningococcal group B** and **group C** capsular polysaccharides. The **group B** and **group C** polysaccharides equally potentiated the antibody response to the serotype 2b protein. Addition of **aluminum hydroxide** or aluminum phosphate markedly improved the antibody response to the serotype 2b protein, but **aluminum hydroxide**-adjuvanted vaccines consistently elicited higher antibody levels. **Aluminum hydroxide**-adsorbed serotype 2a and 2b protein vaccines were evaluated for induction of cross-protective bactericidal antibodies. The 2a vaccines were 2a specific, whereas the 2b vaccines elicited antibodies strongly bactericidal for both 2a and 2b **meningococcal** strains and protected against bacteremia in a mouse model. It may therefore be possible to provide protection against both 2a and 2b disease by using an **aluminum hydroxide**-adsorbed protein vaccine containing a single serotype 2 protein component.

(FILE 'HCAPLUS' ENTERED AT 10:32:05 ON 14 MAR 2003)

L1 2021 SEA FILE=HCAPLUS ABB=ON PLU=ON NMC OR MENC OR (NM OR MEN OR MENINGOCOCC## OR MENINGITID?)(S)((GROUP OR SEROGROUP)(W)C)

L2 1079 SEA FILE=HCAPLUS ABB=ON PLU=ON NMB OR MENB OR (NM OR MEN OR MENINGOCOCC## OR MENINGITID?)(S)((GROUP OR SEROGROUP)(W)B)

L5 332 SEA FILE=REGISTRY ABB=ON PLU=ON ALUMINUM HYDROXIDE?/CN

L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON "MF 59"/CN

L7 2 SEA FILE=REGISTRY ABB=ON PLU=ON ALUM/CN

L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON ALHYDROGEL/CN

L9 335 SEA FILE=REGISTRY ABB=ON PLU=ON L5 OR L6 OR L7 OR L8

L20 131 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR GCM) AND (L2 OR GBM)

L21 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND (L9 OR ALUM OR (AL OR ALUMIN?)(W)(OH OR HYDROXIDE) OR ALOH# OR ALHYDROGEL OR ALHYDRO GEL OR MF59 OR MF 59)

L22 0 L21 NOT L15

Searcher : Shears 308-4994

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:34:16 ON 14 MAR 2003)

L23 23 S L21
L24 0 S L23 NOT L18

(FILE 'HCAPLUS' ENTERED AT 10:35:50 ON 14 MAR 2003)

L5 332 SEA FILE=REGISTRY ABB=ON PLU=ON ALUMINUM HYDROXIDE?/CN

L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON "MF 59"/CN
L7 2 SEA FILE=REGISTRY ABB=ON PLU=ON ALUM/CN
L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON ALHYDROGEL/CN
L9 335 SEA FILE=REGISTRY ABB=ON PLU=ON L5 OR L6 OR L7 OR L8
L26 135 SEA FILE=HCAPLUS ABB=ON PLU=ON (MENINGOCOCC## OR MENINGITID? OR (MEN OR NM)(S)MENING?)(S)(B(3A)C)
L27 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND (L9 OR ALUM OR (AL OR ALUMIN?)(W)(OH OR HYDROXIDE) OR ALOH# OR ALHYDROGEL OR ALHYDRO GEL OR MF59 OR MF 59)

L28 2 L27 NOT L15

L28 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:520216 HCAPLUS
DOCUMENT NUMBER: 136:230824
TITLE: Modulation of the serological response to meningococcal polysaccharides by cytokines
AUTHOR(S): Cortes-Castillo, M. d. l. A.; Thorpe, R.; Corbel, M. J.
CORPORATE SOURCE: Division of Bacteriology, National Institute for Biological Standards and Control, Hertfordshire, EN6 3QG, UK
SOURCE: Vaccine (2001), 19(30), 4194-4203
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Meningococcal** A and **C** but not **B** capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with **aluminum hydroxide** and outer membrane proteins. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/+) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:455406 HCAPLUS
DOCUMENT NUMBER: 111:55406
TITLE: Protective activity of detoxified lipopolysaccharide of Neisseria meningitidis, serogroup A, in in vivo experiments
AUTHOR(S): Del'vig, A. A.; Krasnoproshina, L. I.; Bobyleva, G. V.; Kuvakina, V. I.
CORPORATE SOURCE: Mosk. NII Epidemiol. Mikrobiol., Moscow, USSR
SOURCE: Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (1989), (5), 69-73
CODEN: ZMEIAV; ISSN: 0372-9311
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The immunogenic potency, toxicity, homologous and heterologous protective activity of lipopolysaccharide prepns. obtained from serogroup A N. meningitidis (LPS A) were studied in animal expts. These prepns. had very high protective activity. The alk. treatment of native LPS A decreased the toxicity of the prepn. almost 20-fold and did not affect its immunogenic potency. Detoxified LPS A was capable of protecting mice from fatal meningococcemia resulting from infection with N. **meningitidis** strains, serogroups A, **B**, and **C**; the adsorption of the prepn. on **aluminum hydroxide** did not affect its protective activity. In view of the properties of detoxified LPS A it may be regarded as a possible vaccine prepn.

IT **21645-51-2, Aluminum hydroxide,** biological studies
RL: BIOL (Biological study)
(detoxified Neisseria meningitidis serogroup A lipopolysaccharide adsorption on, protective activity response to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:39:39 ON 14 MAR 2003)
L29 25 S L27
L30 12 S L29 NOT L18
L31 7 DUP REM L30 (5 DUPLICATES REMOVED)

L31 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:592988 BIOSIS
DOCUMENT NUMBER: PREV200200592988
TITLE: Physico-chemical and immunological examination of the thermal stability of tetanus toxoid conjugate vaccines.
AUTHOR(S): Ho, Mei M. (1); Mawas, Fatme; Bolgiano, Barbara; Lemercinier, Xavier; Crane, Dennis T.; Huskisson, Rachel; Corbel, Michael J.
CORPORATE SOURCE: (1) Bacteriology Division, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Herts, EN6 3QG: mho@nibsc.ac.uk UK
SOURCE: Vaccine, (4 October, 2002) Vol. 20, No. 29-30, pp. 3509-3522. http://www.elsevier.com/locate/vaccine.
print.
ISSN: 0264-410X.

DOCUMENT TYPE: Article
LANGUAGE: English
AB The thermal stability of meningococcal C (MenC)- and Haemophilus influenzae b (Hib)-tetanus toxoid (TT) conjugate vaccines was investigated using spectroscopic and chromatographic techniques and immunogenicity assays in animal models. In this stability study, both the bulk concentrate and final fills were incubated at -20, 4, 23, 37 or 55degreeC for 5 weeks or subjected to cycles of freeze-thawing. The structural stability, hydrodynamic size and molecular integrity of the treated vaccines were monitored by circular dichroism (CD), fluorescence and nuclear magnetic resonance (NMR) spectroscopic techniques, size exclusion chromatography (FPLC-SEC), and high performance anion exchange chromatography coupled with pulsed amperometric detection (HPAEC-PAD). Only storage at 55degreeC for 5 weeks caused some slight unfolding and modification in the tertiary structure of the carrier protein in the MenC-TT conjugate. Substantial loss of saccharide content from the MenC conjugates was observed at 37 and 55degreeC. Unexpectedly, the experimental immunogenicity of MenC-TT vaccine adsorbed to **Alhydrogel** was significantly reduced only by repeated freeze-thawing, but not significantly decreased by thermal denaturation. Neither the molecular integrity nor the immunogenicity of the lyophilised Hib-TT vaccines was significantly affected by freeze-thawing or by storage at high temperature. In conclusion, the MenC- and Hib-TT conjugate vaccines were relatively stable when stored at higher temperatures, though when MenC-TT vaccine was adsorbed to **Alhydrogel**, it was more vulnerable to repeated freeze-thawing. When compared with CRM197 conjugate vaccines studied previously using similar techniques (1-3), the tetanus toxoid conjugates were found to have higher relative thermal stability in that they retained immunogenicity following storage at elevated temperatures.

L31 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 1
ACCESSION NUMBER: 2001:386007 BIOSIS
DOCUMENT NUMBER: PREV200100386007
TITLE: Modulation of the serological response to meningococcal polysaccharides by cytokines.
AUTHOR(S): Cortes-Castillo, Maria de los Angeles; Thorpe, R.; Corbel, M. J. (1)
CORPORATE SOURCE: (1) Division of Bacteriology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG: mcorbel@nibsc.ac.uk UK
SOURCE: Vaccine, (20 July, 2001) Vol. 19, No. 30, pp. 4194-4203. print.
ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Meningococcal** A and **C** but not **B** capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in

both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with **aluminium hydroxide** and outer membrane proteins. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/+) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

L31 ANSWER 3 OF 7 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-270574 [23] WPIDS
DOC. NO. CPI: C2000-082483
TITLE: New conjugate of saccharide and protein, used as immunogen and in vaccines, e.g. against bacteria or tumors.
DERWENT CLASS: B04 D16
INVENTOR(S): HUANG, C; MICHON, F; UITZ, C
PATENT ASSIGNEE(S): (NAVA-N) NORTH AMERICAN VACCINE INC; (BAXT-N) BAXTER BIOTECH AG; (BAXT-N) BAXTER BIOTECH TECHNOLOGY SARL
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000010599	A2	20000302	(200023)*	EN	42
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9957800	A	20000314	(200031)		
NO 2001000805	A	20010403	(200128)		
EP 1109576	A2	20010627	(200137)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI					
HU 2001003100	A2	20011128	(200209)		
KR 2001072776	A	20010731	(200209)		
CZ 2001000622	A3	20020116	(200215)		
CN 1323221	A	20011121	(200218)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000010599	A2	WO 1999-US18982	19990818
AU 9957800	A	AU 1999-57800	19990818
NO 2001000805	A	WO 1999-US18982	19990818
		NO 2001-805	20010216
EP 1109576	A2	EP 1999-945115	19990818
		WO 1999-US18982	19990818
HU 2001003100	A2	WO 1999-US18982	19990818
		HU 2001-3100	19990818

KR 2001072776 A	KR 2001-702108	20010219
CZ 2001000622 A3	WO 1999-US18982	19990818
	CZ 2001-622	19990818
CN 1323221 A	CN 1999-812170	19990818

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9957800	A	Based on	WO 200010599
EP 1109576	A2	Based on	WO 200010599
HU 2001003100	A2	Based on	WO 200010599
CZ 2001000622	A3	Based on	WO 200010599

PRIORITY APPLN. INFO: US 1999-376911 19990818; US 1998-97120P 19980819

AN 2000-270574 [23] WPIDS

AB WO 200010599 A UPAB: 20000818

NOVELTY - Conjugate (A) comprises an N-propionated poly- or oligo-saccharide (I) conjugated directly to a protein (II) at the beta -position of the propionate residue is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) method for producing (A);

(2) pharmaceutical composition containing (A) and a carrier;

(3) immunogen, able to produce a (I)-specific immune response, containing (A);

(4) protective vaccines containing (A), and

(5) isolated antibody (Ab), or its antigen-binding fragments, elicited by (A) and immunologically reactive with both (I) and the native N-acetylated saccharide from which (I) is derived.

ACTIVITY - Antibacterial: antifungal; anticancer.

MECHANISM OF ACTION - Induction of a specific immune response.

USE - (A) are used in vaccines and as immunogens to produce an immune response (specifically an antibody response) against the cell (bacterium, yeast or cancer) from which (I) is derived, especially against Streptococcus pneumoniae group B; Neisseria menigitidis groups B or C, and Haemophilus influenzae type B. They may also be used (not claimed) as reagents for detecting antibodies, e.g. for detecting prior exposure to pathogens and to identify subjects already resistant to infection. Antibodies raised using (A) can be used for passive immunization also (not claimed) to detect (I)-expressing cells.

ADVANTAGE - (A) can be produced simply, rapidly, reproducibly and on a large scale, with high yield and efficiency, from a wide variety of (I). Many (I) can be attached to a single (II) and (I) is not altered at a functional group that may be critical for immunogenicity.

Dwg.0/1

L31 ANSWER 4 OF 7 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2000-205407 [18] WPIDS

DOC. NO. CPI: C2000-063253

TITLE: Microparticles with adsorbent surface comprising polymer and detergent, used as vaccines, and for targeted delivery of e.g. polypeptides, efficient adsorbance of biologically active macromolecules.

DERWENT CLASS: A14 A23 A26 A96 B04 B07 C03 D16

INVENTOR(S): BARACKMAN, J; KAZZAZ, J; O'HAGEN, D; OTT, G S; SINGH, M
PATENT ASSIGNEE(S): (CHIR) CHIRON CORP
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000006123	A1	20000210	(200018)*	EN	59
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9952452	A	20000221	(200029)		
EP 1100468	A1	20010523	(200130)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002521425	W	20020716	(200261)		73

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000006123	A1	WO 1999-US17308	19990729
AU 9952452	A	AU 1999-52452	19990729
EP 1100468	A1	EP 1999-937664	19990729
		WO 1999-US17308	19990729
JP 2002521425	W	WO 1999-US17308	19990729
		JP 2000-561979	19990729

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9952452	A	Based on	WO 200006123
EP 1100468	A1	Based on	WO 200006123
JP 2002521425	W	Based on	WO 200006123

PRIORITY APPLN. INFO: US 1999-285855 19990402; US 1998-124533 19980729

AN 2000-205407 [18] WPIDS

AB WO 200006123 A UPAB: 20000412

NOVELTY - Microparticles with an adsorbent surface are new and comprise:

(1) polymer chosen from poly(alpha -hydroxy acid), polyhydroxy butyric acid, polycaprolactone, polyorthoester, polyanhydride or polycyanoacrylate; and

(2) detergent.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of producing microparticles with adsorbent surface to which biologically active macromolecule has been adsorbed.

ACTIVITY - Vaccine; immunomodulating. Microparticle induction of immune response was examined in guinea pigs following intramuscular immunization. Five formulations were tested: (1) PLG/CTAB gp 120 adsorbed (25 mu g); (2) PLG/CTAB gp 120 adsorbed (25 mu g) + aluminum phosphate; (3) soluble gp 120 DNA (25 mu g) +

aluminum phosphate; (4) soluble gp 120 DNA (25 mu g) alone; and (5) **MF59** protein (50 mg). GMT of serum was as follows: (1) 1,435 plus or minus 383; (2) 3,624 plus or minus 454; (3) 119 plus or minus 606; (4) 101 plus or minus 55; and (5) 3,468 plus or minus 911. Antibody induction (collection and analysis of serum) were performed and geometric mean titer of serum determined.

USE - Used for diagnosis or treatment of disease, as vaccines and to raise and immune response. Used to deliver polypeptides, polynucleotides, polynucleosides, antigens, pharmaceuticals, hormones, enzymes, transcription or translation mediators, intermediates in metabolic pathway, immunomodulators or adjuvants including aluminum salts (claimed) such as double- and single stranded sequences including cDNA, prokaryotic or eukaryotic mRNA, genomic RNA and DNA sequences form viral or prokaryotic DNA (RNA and DNA viruses), and synthetic DNA sequences, base analogs of DNA and RNA, antibiotics, antivirals, peptides, oligopeptides, dimers, multimers, antigens derived from bacteria (Bordetella pertussis, Neisseria **meningitides** (A, **B**, **C**, Y), Neisseria gonorrhoeae, Helicobacter pylori and/or Haemophilus influenzae), viruses, parasites, fungi and tumors, non-steroidal anti-inflammatory drugs, analgesics, vasodilators, cardiovascular drugs, psychotropics, neuroleptics, antidepressants, anti-Parkinson drugs, beta blockers, calcium channel blockers, bradykinin inhibitors, angiotensin-converting enzyme inhibitors, prolactin inhibitors, steroids, hormone antagonists, antihistamines, serotonin antagonists, heparin, chemotherapeutic agents, antineoplastics and growth factors (platelet derived growth factor (PDGF), epithelial growth factor (EGF), KGF, insulin-like growth factor (IGF)-1, IFG-2), FGF, polynucleotides that encode therapeutic or immunogenic proteins, immunogenic proteins and epitopes for use in vaccines, hormones including peptide hormones (insulin, proinsulin, growth hormone, GHRH, luteinizing hormone releasing hormone (LHRH), EGF, somatostatin, SNX-111, BNP, insulinotropin, ANP, FSH, LH, PSH and hCG), gonadal steroid hormones (androgens, estrogens, progesterone), thyroid-stimulating hormone, inhibin, cholecystokinin, ACTH, CRF, dynorphins, endorphins, endothelin, fibronectin fragments, galanin, gastrin, glucagons, GTP-binding protein fragments, guanylin, leukokinins, magainin, mastoparans, dermaseptin, systemin, neuromedin, neurotensin, pancreastatin, pancreatic polypeptide, substance P, secretin, thymosin, and cytokines (interleukin (IL) 1, IL-2, IL-3, IL-4 and gamma interferon). Used for site-specific targeted delivery.

ADVANTAGE - Efficiently adsorb biologically active macromolecules such as DNA, polypeptides, antigens and adjuvants. Capable of adsorbing wide variety of macromolecules. Flexible delivery systems, particularly for drugs that are highly sensitive and difficult to formulate.

Dwg.0/0

L31 ANSWER 5 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998040280 EMBASE
TITLE: Meningococcal vaccine development: A novel approach.
AUTHOR: Fusco P.C.; Blake M.S.; Michon F.
CORPORATE SOURCE: P.C. Fusco, North American Vaccine, Inc., 12103 Indian Creek Court, Beltsville, MD 20705, United States
SOURCE: Expert Opinion on Investigational Drugs, (1998) 7/2 (245-252).

Refs: 53
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Neisseria **meningitidis** is a major world-wide cause of meningitis. Effective capsular polysaccharide (CPS) vaccines, that elicit CPS-specific bactericidal (BC) antibodies, were previously developed and licensed to protect against **meningococcal** disease. However, due to their T-cell independent character, CPS vaccines are useless in infants and do not provide immunological memory or long-lasting protection in adults. CPS-protein conjugate vaccines are being developed to improve and broaden vaccine efficacy by creating T-cell dependent antigens. However, group B **meningococci** (GBM) are responsible for nearly half of **meningococcal** disease and possess a CPS, composed a polysialic acid, that is poorly immunogenic. N-propionyl (NPr) modification of the GBM polysaccharide (GBMP) has enhanced its immunogenicity, but BC antibodies are not induced at high levels, even when conjugated to conventional protein carriers, unless adjuvants stronger than **aluminium hydroxide** are used. We have chosen to couple the NPr-GBMP by reductive amination to a recombinant GBM class 3 porin (rPorB), which we have shown to modulate the immune response in animals towards the production of CPS-specific BC antibodies. We have also combined this conjugate with similar CPS-rPorB conjugates for groups A and C **meningococci** to form a trivalent A/**B/C** conjugate vaccine. This trivalent **meningococcal** vaccine has been shown to be safe and highly immunogenic in mice and non human primates, generating CPS-specific BC antibodies for each of the 3 major serogroups, which should provide world-wide protection against **meningococcal** disease.

L31 ANSWER 6 OF 7 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1989-124777 [17] WPIDS
DOC. NO. CPI: C1989-055231
TITLE: Polyvalent vaccine of class 1 adventitia protein of Meningococcus - comprises adventious protein treated with bromo cyanide and incorporating surfactant and/or adsorbent.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (NEDE) DUTCH GOVERNMENT
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 01029321	A	19890131	(198917)*		6
CN 1030443	A	19890118	(198950)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

JP 01029321 A JP 1988-168652 19880706

PRIORITY APPLN. INFO: NL 1987-1600 19870707
AN 1989-124777 [17] WPIDS
AB JP 01029321 A UPAB: 19930923
Vaccine comprises one or more kinds of segments of class 1 adventitia protein of **meningococcus**. Vaccin, comprises one or more kinds of segments of class 1 A, **B**, **C**, W and/or Y adventitia protein of **meningococcus**. Pref. the protein is treated with bromocyanide. Pref. the protein segment has mol. wt. of 2000 to 25000 D. Pref. the segment is obtd. by protein decomposition at end Arg-C, end Glu-C. Pref. the protein is polypeptide is FSGFSGSVQFV or PIQNSKSAYTP.

Vaccine incorporates nonion, anion, cation or amphoteric surfactant and/or adsorbent selected fromaluminium phosphate, **aluminium hydroxide** ane calcium phosphate.
(Provisional Basic previously advised in week 8910)
0/0

L31 ANSWER 7 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 89389589 MEDLINE
DOCUMENT NUMBER: 89389589 PubMed ID: 2506720
TITLE: [The protective activity of the detoxified lipopolysaccharide of Neisseria meningitidis serogroup A in in vivo experiments]. Protektivnaia aktivnost' detoksitsirovannogo lipopolisakharida Neisseria meningitidis serogruppy A v opytakh in vivo.
AUTHOR: Del'vig A A; Krasnoproshina L I; Bobyleva G V; Kuvakina V I
SOURCE: ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1989 May) (5) 69-73. Journal code: 0415217. ISSN: 0372-9311.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891026

AB The immunogenic potency, toxicity, homologous and heterologous protective activity of lipopolysaccharide preparations obtained from serogroup A N. **meningitidis** (LPS A) were studied in animal experiments. These preparations were shown to possess very high protective activity. The alkaline treatment of native LPS A decreased the toxicity of the preparation almost 20 times and did not affect its immunogenic potency. Detoxified LPS A was capable of protecting mice from fatal meningococcemia resulting from infection with N. **meningitidis** strains, serogroups A, **B** and **C**; the adsorption of the preparation on **aluminium hydroxide** did not affect its protective activity. In view of the properties of detoxified LPS A revealed in this investigation, it may be regarded as a possible vaccinal preparation.

(FILE 'MEDLINE' ENTERED AT 10:41:02 ON 14 MAR 2003)

L32 12 SEA FILE=MEDLINE ABB=ON PLU=ON "NEISSERIA MENINGITIDIS, SEROGROUP B"/CT
L33 17 SEA FILE=MEDLINE ABB=ON PLU=ON "NEISSERIA MENINGITIDIS, SEROGROUP C"/CT
L34 5 SEA FILE=MEDLINE ABB=ON PLU=ON L32 AND L33

L34 ANSWER 1 OF 5 MEDLINE
AN 2003087792 MEDLINE
TI Immune response to native NadA from Neisseria meningitidis and its expression in clinical isolates in Brazil.
AU Fukasawa Lucila O; Gorla Maria Cecilia O; Lemos Ana Paula S; Schenkman Rocilda P F; Brandileone Maria Cristina C; Fox Jay W; Raw Isaias; Frasch Carl E; Tanizaki Martha M
SO JOURNAL OF MEDICAL MICROBIOLOGY, (2003 Feb) 52 (Pt 2) 121-5. Journal code: 0224131. ISSN: 0022-2615.
AB A mAb against the NadA protein from Neisseria meningitidis strain 3006 (serosubtype B : 2b : P1.2 : P5.2,8) demonstrated strong bactericidal activity against Brazilian epidemic serogroup B strain N44/89 (B : 4,7 : P1.19,15 : P5.5,7) and a serogroup C strain, IMC 2135 (C : 2a : P1.5,2), but not against another serogroup C strain, N1002/90 (C : 2b : P1.3 : P5.8). The immunogenicity of native NadA in an outer-membrane vesicle (OMV) preparation was also tested. Serum from mice immunized with OMV from serogroup B strain N44/89, which contains the NadA protein, showed bactericidal activity against serogroup B and C strains possessing NadA. In dot-blot analysis of 100 serogroup B and 100 serogroup C isolates from Brazilian patients, the mAb to NadA recognized about 60 % of the samples from both serogroups. The molecular mass of the NadA protein from strain N44/89 determined by mass spectrometry was 37 971 Da and the peptide sequences were identical to those of NadA from N. meningitidis strain MC58.

L34 ANSWER 2 OF 5 MEDLINE
AN 2002674719 MEDLINE
TI Estimating the burden of serogroup C meningococcal disease in England and Wales.
AU Davison K L; Ramsay M E; Crowcroft N S; Lieftucht A; Kaczmarski E B; Trotter C L; Gungabissoon U; Begg N T
SO COMMUNICABLE DISEASE AND PUBLIC HEALTH, (2002 Sep) 5 (3) 213-9. Journal code: 9808711.
AB In 1999 a new conjugate vaccine for serogroup C meningococcal disease was licensed for use in the UK. In order for an appropriate vaccination strategy to be developed the burden of serogroup C disease in England and Wales needed to be established. This was done using data from an enhanced surveillance scheme alongside routine laboratory reports and a total of 5,052 cases of serogroup C disease in England and Wales between 1993 and 1998 were estimated. Among these, an estimated 398 died and 1,767 were admitted to intensive care units (ITUs). The greatest burden of disease was in young children and teenagers. The current literature identified four studies reporting sequelae following serogroup C meningococcal disease. These provided estimates of sequelae in the range of 6.5% and 45% and presented some evidence of higher levels than occur following serogroup B meningococcal disease. This information was provided to the Joint Committee on Vaccination and Immunisation to inform policy to implement a serogroup C conjugate vaccination programme in the UK. The vaccination programme has since been justified by the dramatic reduction in serogroup C meningococcal

cases.

L34 ANSWER 3 OF 5 MEDLINE
AN 2002650075 MEDLINE
TI Rates of detection of Neisseria meningitidis in tonsils differ in relation to local incidence of invasive disease.
AU Greiner Oliver; Berger Christoph; Day Philip J R; Meier Gabriela; Tang Christoph M; Nadal David
SO JOURNAL OF CLINICAL MICROBIOLOGY, (2002 Nov) 40 (11) 3917-21. Journal code: 7505564. ISSN: 0095-1137.
AB Nasopharyngeal swabbing substantially underestimates carriage of Neisseria meningitidis. Real-time PCR assays were employed to examine the presence of a broad range of bacteria and of N. meningitidis groups B and C, respectively, in tonsils from 26 individuals from Oxford, England, and 72 individuals from Zurich, Switzerland. The detection limit of each PCR system was DNA from one bacterial cell per reaction mixture. Tonsillar DNA did not inhibit amplification of meningococcal gene sequences, and N. meningitidis was detected in tonsils exposed to the bacterium. Whereas in both sets of patients other bacteria were detected, N. meningitidis group B and group C were only found in tonsils from Oxford where the incidence of invasive meningococcal disease is much higher than in Zurich. These observations suggest that PCR-based methods could be used for the detection of meningococcal carriage and that difference in disease incidence could be explained by different transmission rates in the community rather than host genetics or coexisting infections.

L34 ANSWER 4 OF 5 MEDLINE
AN 2002328478 MEDLINE
TI A case of meningococcal disease in a schoolgirl previously given meningococcal C vaccine.
AU Pugh R N; Heseltine A
SO COMMUNICABLE DISEASE AND PUBLIC HEALTH, (2002 Mar) 5 (1) 74. Journal code: 9808711.

L34 ANSWER 5 OF 5 MEDLINE
AN 2002321895 MEDLINE
TI The changing epidemiology of bacterial meningitis and invasive non-meningitic bacterial disease in scotland during the period 1983-99.
AU Kyaw Moe H; Christie Peter; Jones Ian G; Campbell Harry
SO SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (2002) 34 (4) 289-98. Journal code: 0215333. ISSN: 0036-5548.
AB We reviewed population-based laboratory reports of invasive meningococcal, pneumococcal, Haemophilus influenzae, Group B Streptococcus (GBS) and Listeria monocytogenes isolates in order to examine the changing epidemiology of meningitis and invasive non-meningitic disease (INMD) caused by these 5 pathogens in the 2 periods before (1983-91) and after (1992-99) routine use of H. influenzae type B conjugate vaccine (Hib) in Scotland. Neissieria meningitidis was the most common cause of meningitis, accounting for 39.2% of cases of meningitis in 1983-91 and 47% of cases in 1992-99, followed by H. influenzae (31%), Streptococcus pneumoniae (22.4%), GBS (3.9%) and L. monocytogenes (3.5%) in 1983-91 and S. pneumoniae (36.3%), H. influenzae (7.8%), GBS (6.1%) and L. monocytogenes (2.8%) in 1992-99. The important epidemiological features of meningitis and INMD caused by these 5 pathogens between 1983-91 and

1992-99 include: 1. The incidence of bacterial meningitis due to S. pneumoniae and GBS was stable; 2. S. pneumoniae was the predominant cause of INMD in both periods; 3. The incidences of INMD caused by N. meningitidis, GBS and S. pneumoniae increased, by 27%, 55% and 56%, respectively; 4. Decreases in the incidences of bacterial meningitis (by 50%) and INMD (by 50%) due to L. monocytogenes were detected; and 5. There were dramatic reductions in the proportions of bacterial meningitis (by 92%) and INMD (by 56%) due to H. influenzae in vaccinated and non-vaccinated individuals. Continued surveillance is necessary to monitor the disease trend, population at risk, serotype distribution and antimicrobial susceptibility in order to implement appropriate public health interventions against invasive bacterial disease.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER' ENTERED AT 10:42:03 ON 14 MAR 2003)

L35	706	SEA	ABB=ON	PLU=ON	"GRANOFF D"?/AU
L36	703	SEA	ABB=ON	PLU=ON	"RAFF H"?/AU
L37	139	SEA	ABB=ON	PLU=ON	"AABERGE I"?/AU
L38	353	SEA	ABB=ON	PLU=ON	"HANEBERG B"?/AU
L39	2911	SEA	ABB=ON	PLU=ON	"HOLST J"?/AU
L40	2	SEA	ABB=ON	PLU=ON	L35 AND L36 AND L37 AND L38 AND L39
L41	19	SEA	ABB=ON	PLU=ON	L35 AND (L36 OR L37 OR L38 OR L39)
L42	2	SEA	ABB=ON	PLU=ON	L36 AND (L37 OR L38 OR L39)
L43	27	SEA	ABB=ON	PLU=ON	L37 AND (L38 OR L39)
L44	52	SEA	ABB=ON	PLU=ON	L38 AND L39
L45	23	SEA	ABB=ON	PLU=ON	(L43 OR L44 OR L35 OR L36 OR L37 OR L38 OR L39) AND (L20 OR L26)
L46	40	SEA	ABB=ON	PLU=ON	L40 OR L41 OR L42 OR L45
L47	15	DUP	REM L46	(25 DUPLICATES REMOVED)	

L47 ANSWER 1 OF 15 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2002248857 MEDLINE
DOCUMENT NUMBER: 21984360 PubMed ID: 11988262
TITLE: Development of vaccines against meningococcal disease.
AUTHOR: Jodar Luis; Feavers Ian M; Salisbury David; **Granoff Dan M**
CORPORATE SOURCE: Vaccine Development and Quality and Safety of Biologicals, World Health Organization, Geneva, Switzerland.. jodar@who.org
CONTRACT NUMBER: AI45642 (NIAID)
AI46464 (NIAID)
SOURCE: LANCET, (2002 Apr 27) 359 (9316) 1499-508. Ref: 165
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020505
Last Updated on STN: 20020528
Entered Medline: 20020522

AB Neisseria **meningitidis** is a major cause of bacterial meningitis and sepsis. Polysaccharide-protein conjugate vaccines for

prevention of **group C** disease have been licensed in Europe. Such vaccines for prevention of disease caused by groups A (which is associated with the greatest disease burden worldwide), Y, and W135 are being developed. However, conventional approaches to develop a vaccine for **group B** strains, which are responsible for most cases in Europe and the USA, have been largely unsuccessful. Capsular polysaccharide-based vaccines can elicit autoantibodies to host polysialic acid, whereas the ability of most non-capsular antigens to elicit broad-based immunity is limited by their antigenic diversity. Many new membrane proteins have been discovered during analyses of genomic sequencing data. These antigens are highly conserved and, in mice, elicit serum bactericidal antibodies, which are the serological hallmark of protective immunity in man. Therefore, there are many promising new vaccine candidates, and improved prospects for development of a broadly protective vaccine for **group B** disease, and for control of all **meningococcal** disease.

L47 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 1999:763897 HCAPLUS
DOCUMENT NUMBER: 132:15578
TITLE: Combination **meningitidis B/C** vaccines
INVENTOR(S): **Granoff, Dan M.; Aaberge, Ingeborg S.; Haneberg, Bjorn; Holst, Johan; Raff, Howard**
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961053	A1	19991202	WO 1999-US11977	19990528
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2332963	AA	19991202	CA 1999-2332963	19990528
AU 9942215	A1	19991213	AU 1999-42215	19990528
BR 9910749	A	20010213	BR 1999-10749	19990528
EP 1079857	A1	20010307	EP 1999-926046	19990528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002516292	T2	20020604	JP 2000-550512	19990528

PRIORITY APPLN. INFO.:			
US 1998-87351P	P	19980529	
US 1998-106446P	P	19981030	
WO 1999-US11977	W	19990528	

AB A combination vaccine for Neisseria **meningitidis** (**Nm**) comprising outer membrane proteins from

serogroup B and oligosaccharides from **serogroup C**, and its use for the prevention or treatment of disease is disclosed. Pigs were injected with two injection of **NmC** conjugate/**NmB**/MF59 (10.mu.g/25.mu.g/0.5 mL) sepd. by 28 days. The combination vaccine immunogenic as measured by **NmB** and **NmC** IgG antibody titers, resp. The antibody response induced by the combination vaccine was significantly greater than the antibody response induced by either the **NmC** conjugate alone, or the combination of **NmC** conjugate and **NmB** in the presence of alum. When adjuvant MF59 was present, the antibody titer for the combination vaccine increased approx. six-fold.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1999:709841 HCAPLUS
DOCUMENT NUMBER: 132:319566
TITLE: Differences in surface expression of NspA among Neisseria meningitidis group B strains
AUTHOR(S): Moe, Gregory R.; Tan, Siqi; **Granoff, Dan M.**
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, Oakland, CA, 94609, USA
SOURCE: Infection and Immunity (1999), 67(11), 5664-5675
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NspA is a highly conserved membrane protein that is reported to elicit protective antibody responses against Neisseria **meningitidis** serogroups A, **B** and **C** in mice. To investigate the vaccine potential of NspA, we produced mouse antirecombinant NspA (rNspA) antisera, which were used to evaluate the accessibility of NspA epitopes on the surface of different serogroup B strains by an immunofluorescence flow cytometric assay and by susceptibility to antibody-dependent, complement-mediated bacteriolysis. Among 17 genetically diverse strains tested, 11 (65%) were pos. for NspA cell surface epitopes and 6 (35%) were neg. All six neg. strains also were resistant to bactericidal activity induced by the anti-rNspA antiserum. In contrast, of the 11 NspA surface-pos. strains, 8 (73%; $P < 0.05$) were killed by the antiserum and complement. In infant rats challenged with one of these eight strains, the anti-rNspA antiserum conferred protection against bacteremia, whereas the antiserum failed to protect rats challenged by one of the six NspA cell surface-neg. strains. Neither NspA expression nor protein sequence accounted for differences in NspA surface accessibility, since all six neg. strains expressed NspA in outer membrane prepns. and since their predicted NspA amino acid sequences were 99 to 100% identical to those of three representative pos. strains. However, the six NspA cell surface-neg. strains produced, on av., larger amts. of group B polysaccharide than did the 11 pos. strains (reciprocal geometric mean titers, 676 and 224, resp.; $P < 0.05$), which suggests that the capsule may limit the accessibility of NspA surface epitopes. Given these strain differences in NspA surface accessibility, an rNspA-based meningococcal B vaccine may have to be

supplemented by addnl. antigens.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:281611 BIOSIS
DOCUMENT NUMBER: PREV199800281611
TITLE: Effect of aluminium hydroxide and **meningococcal serogroup C** capsular polysaccharide on the immunogenicity and reactogenicity of a **group B** Neisseria **meningitidis** outer membrane vesicle vaccine.
AUTHOR(S): Rosenqvist, E. (1); Hoiby, E. A.; Bjune, G.; Aase, A.; Halstensen, A.; Lehmann, A. K.; Paulssen, J.; **Holst, J.**; Michaelsen, T. E.; Nokleby, H.; Froholm, L. O.; Closs, O.
CORPORATE SOURCE: (1) Dep. Vaccinol., Natl. Inst. Public Health, P.O. Box 4404 Torshov, N-0403 Oslo Norway
SOURCE: Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 323-333. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens.
Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization
. ISSN: 0301-5149. ISBN: 3-8055-6640-9.
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L47 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:507859 HCAPLUS
DOCUMENT NUMBER: 129:259071
TITLE: A modified enzyme-linked immunosorbent assay for measurement of antibody responses to meningococcal C polysaccharide that correlate with bactericidal responses
AUTHOR(S): **Granoff, Dan M.**; Maslanka, Susan E.; Carlone, George M.; Plikaytis, Brian D.; Santos, George F.; Mokatrin, Ahmad; **Raff, Howard V.**
CORPORATE SOURCE: Chiron Vaccines, Emeryville, CA, 94608-2916, USA
SOURCE: Clinical and Diagnostic Laboratory Immunology (1998), 5(4), 479-485
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The standardized ELISA for measurement of serum IgG antibody responses to meningococcal C polysaccharide has been modified to employ assay conditions that ensure specificity and favor detection primarily of high-avidity antibodies. The modified and std. assays were used to measure IgG antibody concns. in sera of toddlers vaccinated with meningococcal polysaccharide vaccine or a

meningococcal C conjugate vaccine. The results were compared to the resp. complement-mediated bactericidal antibody titers. In sera obtained after 1 or 2 doses of vaccine, the correlation coeffs., for the results of the std. assay and bactericidal antibody titers were 0.45 and 0.29, compared to 0.85 and 0.87, resp., for the modified assay. With the std. assay, there were no differences between the geometric mean antibody responses of the 2 vaccine groups. In contrast, with the modified assay, 5-20-fold higher postvaccination antibody concns. were measured in the conjugate than in the polysaccharide group. Importantly, the results of the modified assay, but not the std. ELISA, paralleled the resp. geometric mean bactericidal antibody titers. Thus, by employing conditions that favor detection of higher-avidity IgG antibody, the modified ELISA provides results that correlate closely with measurements of antibody functional activity that are thought to be important in protection against meningococcal disease.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5

ACCESSION NUMBER: 1998:340244 HCAPLUS

DOCUMENT NUMBER: 129:121375

TITLE: Effect of aluminum hydroxide and **meningococcal serogroup C** capsular polysaccharide on the immunogenicity and reactogenicity of a **group B** Neisseria **meningitidis** outer membrane vesicle vaccine

AUTHOR(S): Rosenqvist, E.; Hoiby, E. A.; Bjune, G.; Aase, A.; Halstensen, A.; Lehmann, A. K.; Paulssen, J.; **Holst, J.**; Michaelsen, T. E.; Nokleby, H.; Froholm, L. O.; Closs, O.

CORPORATE SOURCE: Departments of Vaccinology and Bacteriology, National Institute of Public Health, Oslo, Norway

SOURCE: Developments in Biological Standardization (1998), 92(Modulation of the Immune Response to Vaccine Antigens), 323-333
CODEN: DVBSA3; ISSN: 0301-5149

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three different formulations of an outer membrane vesicle (OMV) vaccine against **group B meningococcal** disease have been prepd. and tested for immunogenicity and reactogenicity in adult volunteers. The vaccines were prepd. with or without aluminum hydroxide and serogroup C-polysaccharide (C-ps). Doses from 12.5 to 100 .mu.g protein were given twice at a six weeks' interval. All three formulations were well tolerated and highly immunogenic, inducing bactericidal and opsonizing antibodies in humans. Adsorption of OMVs to aluminum hydroxide reduced the pyrogenicity in rabbits. The differences in immunogenicity between the formulations were relatively small, but after the second dose a stronger booster response was obsd. when the vaccines were adsorbed. Thus, a formulation with OMVs and C-ps represents a safe and highly immunogenic vaccine, even without aluminum hydroxide.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 6
ACCESSION NUMBER: 1997:306965 HCAPLUS
DOCUMENT NUMBER: 127:3884
TITLE: MF59 adjuvant enhances antibody responses of infant baboons immunized with Haemophilus influenzae type b and Neisseria meningitidis group C oligosaccharide-CRM197 conjugate vaccine
AUTHOR(S): **Granoff, Dan M.**; McHugh, Yvonne E.; **Raff, Howard V.**; Mokatrin, Ahmad S.; Van Nest, Gary A.
CORPORATE SOURCE: Chiron Vaccines, Emeryville, CA, 94608, USA
SOURCE: Infection and Immunity (1997), 65(5), 1710-1715
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of the adjuvant MF59 to enhance the immunogenicity of polysaccharide-protein conjugate vaccines was investigated in infant baboons. MF59 consists of stable droplets (<250 nm) of the metabolizable oil squalene and two surfactants, polyoxyethylene sorbitan monooleate and sorbitan trioleate, in an oil-in-water emulsion. In humans, MF59 is well tolerated and enhances the immunogenicity of recombinant protein subunit or particle vaccines. Its effect on the immunogenicity of polysaccharide-protein conjugate vaccines is unknown. Baboons 1-4 mo of age were immunized i.m. with N. meningitidis group C and H. influenzae type b (Hib) oligosaccharide-CRM197 conjugate vaccines. The lyophilized vaccines were reconstituted with phosphate-buffered saline (PBS), Al(OH)3 (alum), or MF59. Groups of 5 animals each were given 3 injections of the resp. formulations, with one injection every 4 wk. Four weeks after each immunization, the MF59 group had up to 7-fold-higher geometric mean anticapsular-antibody titers than the alum group and 5-10-fold higher N. meningitidis group C bactericidal antibody titers. Twenty-one weeks after the 3rd immunization, the MF59 group still showed 5-10-fold-higher anticapsular antibody titers. The antibody responses of the animals given the vaccines reconstituted with PBS were low at all times measured. Both the MF59 and alum groups, but not the PBS group, showed booster antibody responses to unconjugated Hib and N. meningitidis group C polysaccharides, results consistent with induction of memory B cells. Thus, MF59 may be useful for accelerating and augmenting immunity to polysaccharide-protein conjugate vaccines in infants.

L47 ANSWER 8 OF 15 MEDLINE
ACCESSION NUMBER: 97138195 MEDLINE
DOCUMENT NUMBER: 97138195 PubMed ID: 8985221
TITLE: Induction of immunologic memory in Gambian children by vaccination in infancy with a group A plus **group C meningococcal** polysaccharide-protein conjugate vaccine.
AUTHOR: Leach A; Twumasi P A; Kumah S; Banya W S; Jaffar S; Forrest B D; **Granoff D M**; LiButti D E; Carlone G M; Pais L B; Broome C V; Greenwood B M
CORPORATE SOURCE: Medical Research Council Laboratories, Fajara,

Banjul, Gambia.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1997 Jan) 175 (1) 200-4.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970127

AB Two hundred twenty-one Gambian children vaccinated previously with one, two, or three doses of a **meningococcal** conjugate vaccine or two doses of polysaccharide vaccine before the age of 6 months were revaccinated at the age of 18-24 months with either **meningococcal** polysaccharide, conjugate, or inactivated polio vaccines. Children who had previously received one, two, or three doses of conjugate vaccine had significantly ($P < .001$) higher anti-**group C meningococcal** antibody levels following revaccination than did children vaccinated with a polysaccharide vaccine for the first time. Children vaccinated previously with two doses of polysaccharide vaccine had a lower **group C** antibody response than did control children. Group A antibody responses following revaccination of children who had previously received polysaccharide or conjugate vaccine were not significantly higher than those in control children. Thus, immunologic memory was probably induced by the **group C** but not by the group A component of the conjugate vaccine.

L47 ANSWER 9 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:249947 BIOSIS
DOCUMENT NUMBER: PREV199698806076
TITLE: Biocine meningococcal C (MenC) conjugate vaccine elicits high titers of serum bactericidal activity in toddlers.
AUTHOR(S): MacDonald, Noni N. E. (1); Halperin, Scott; Law, Barbara; Forrest, Bruce D.; Mokatrin, Ahmad; **Raff, Howard P.**; Costantino, Paolo; Ceccarini, Costante; **Granoff, Dan M.**
CORPORATE SOURCE: (1) Child. Hosp. Eastern Ont., Ottawa, ON Canada
SOURCE: Pediatric Research, (1996) Vol. 39, No. 4 PART 2, pp. 178A.
Meeting Info.: Joint Meeting of the American Pediatric Society and the Society for Pediatric Research Washington, D.C., USA May 6-10, 1996
ISSN: 0031-3998.
DOCUMENT TYPE: Conference
LANGUAGE: English

L47 ANSWER 10 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:195804 BIOSIS
DOCUMENT NUMBER: PREV199799495007
TITLE: Correlation between ELISA and bactericidal activity in infants and toddlers immunized with a MenC-CRM

conjugate vaccine.
AUTHOR(S): **Raff, H.**; Santos, G.; Moos-Holling, R.; Owens, M.; Forrest, B.; **Granoff, D.**; Biocine, Chiron
CORPORATE SOURCE: Emeryville, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1996) Vol. 36, No. 0, pp. 158.
Meeting Info.: 36th ICAAC (International Conference of Antimicrobial Agents and Chemotherapy) New Orleans, Louisiana, USA September 15-18, 1996
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L47 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:195784 BIOSIS
DOCUMENT NUMBER: PREV199799494987
TITLE: MF59 adjuvant enhances anticapsular antibody responses of infant primates vaccinated with meningococcal C (MenC) and Haemophilus type b (Hib) oligosaccharide (OS)-protein conjugate vaccines.
AUTHOR(S): **Granoff, D. M.**; McHugh, Y. E.; Van Nest, G. A.; **Raff, H.**
CORPORATE SOURCE: Chiron Biocine, Emeryville, CA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1996) Vol. 36, No. 0, pp. 155.
Meeting Info.: 36th ICAAC (International Conference of Antimicrobial Agents and Chemotherapy) New Orleans, Louisiana, USA September 15-18, 1996
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L47 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 1995:522549 HCAPLUS
DOCUMENT NUMBER: 122:288399
TITLE: Human immunoglobulin M paraproteins cross-reactive with Neisseria meningitidis group B polysaccharide and fetal brain
AUTHOR(S): Azmi, Farrukh H.; Lucas, Alexander H.; Spiegelberg, Hans L.; **Granoff, Dan M.**
CORPORATE SOURCE: Children's Hos. Oakland Res. Inst., Oakland, CA, 94609, USA
SOURCE: Infection and Immunity (1995), 63(5), 1906-13
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three hundred fifty-nine serum samples from patients with IgM (IgM) or IgG monoclonal gammopathies were tested for binding to the capsular polysaccharide (PS) of Neisseria meningitidis group B (MenB PS, poly-.alpha.[2.fwdarw.8]-N-acetylneuraminic acid). Of 159 IgM paraproteins, 7 (4.4%) were pos., compared with 0 of 200 IgG paraproteins. Since MenB PS reactivity was limited to the IgM paraproteins, the 159 IgM paraproteins were tested by ELISA for reactivity with seven other bacterial PSs. None reacted with **meningococcal** A or **C**, Haemophilus influenzae type **b**, or Streptococcus pneumoniae type 3, 6, 14, or 23 PS. The

specificity of the MenB PS-reactive antibodies was confirmed by demonstration of binding to N. meningitidis group B cells but not to a capsular PS-deficient mutant and by specific inhibition of binding to solid-phase MenB PS by sol. MenB PS in an ELISA. Five of five antibodies tested protected infant rats from bacteremia caused by Escherichia coli K1, an organism with a PS capsule that also is composed of poly-.alpha.[2.fwdarw.8]-N-acetylneuraminic acid. Each of the seven MenB PS-reactive paraproteins had autoantibody activity as defined by binding to homogenates of calf brain in a RIA. For six of the seven antibodies, binding to calf brain was inhibited by the addn. of sol. MenB PS. Thus, approx. 4% of human IgM paraproteins have autoantibody activity to poly-.alpha.[2.fwdarw.8]-N-acetylneuraminic acid, an antigen expressed in fetal brain and cross-reactive with the MenB capsular PS. The reason for this skewing of the IgM paraprotein repertoire toward reactivity with poly-.alpha.[2.fwdarw.8]-N-acetylneuraminic acid antigenic determinants is unknown.

L47 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
ACCESSION NUMBER: 1995:11102 HCAPLUS
DOCUMENT NUMBER: 122:53560
TITLE: Variable region sequences and idiotypic expression of a protective human immunoglobulin M antibody to capsular polysaccharides of Neisseria meningitidis group B and Escherichia coli K1
AUTHOR(S): Azmi, Farrukh H.; Lucas, Alexander H.; **Raff, Howard V.; Granoff, Dan M.**
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, USA
SOURCE: Infection and Immunity (1994), 62(5), 1776-86
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We detd. the heavy (H)- and light (L)-chain variable (V) region nucleotide and translated amino acid sequences of the human IgM(.kappa.) monoclonal antibody (MAb) 5E1, which is specific for the polysaccharide capsule of Escherichia coli K1 and Neisseria meningitidis group B (poly[.alpha.(2.fwdarw.8)-N-acetylneuraminic acid]) and which is protective in animal models of infection. The 5E1 VH gene is a member of the VHIIIb family and is 97% homologous to the 9.1 germ line gene. The 5E1 VL gene is a member of the .kappa.I subgroup and is 98% homologous to the germ line gene, 15A, also known as KLO12. The VL and/or VH genes used by 5E1 are highly homologous to the V genes encoding antibodies to the Haemophilus influenzae type b polysaccharide and to antibodies reactive with self-antigens such as erythrocyte "i," DNA, and thyroid peroxidase. We also produced three murine anti-idiotype (Id) MAbs against 5E1. All three anti-Ids recognize a minor subset of antimeningococcal B polysaccharide antibodies present in serum from normal adults. Two of the anti-Ids define distinct Ids assocd. with antibodies having .kappa.I-15A V regions. These 15A-assocd. Ids are expressed by some heterologous human antimeningococcal B polysaccharide MAbs, and they also are independently expressed by two human MAbs that are specific for either the H. influenzae b polysaccharide or the i erythrocyte antigen and that utilize the .kappa.I-15A V region. Taken together, these data indicate that the 5E1 antibody uses V regions that recur in the human antibody repertoires to this polysaccharide and to structurally dissimilar polysaccharides and autoantigens. Thus, the

poor immunogenicity of poly[.alpha.(2.fwdarw.8)-N-acetylneuraminic acid] cannot be explained by the unavailability of certain crit. VH and VL genes required for generation of antibody response.

L47 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:247921 BIOSIS
DOCUMENT NUMBER: PREV199497260921
TITLE: Variable region sequences and idiotypic expression of protective human IgM antibody to the capsular polysaccharide of Neisseria meningitidis group B.
AUTHOR(S): Azmi, F. H. (1); Lucas, A. H.; **Raff, H. V.**; **Granoff, D. M.**
CORPORATE SOURCE: (1) Child. Hosp., Oakland Res. Inst., Oakland, CA USA
SOURCE: Pediatric Research, (1994) Vol. 35, No. 4 PART 2, pp. 9A.
Meeting Info.: 104th Annual Meeting of the American Pediatric Society and the 63rd Annual Meeting of the Society for Pediatric Research Seattle, Washington, USA May 2-5, 1994
ISSN: 0031-3998.
DOCUMENT TYPE: Conference
LANGUAGE: English

L47 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 9
ACCESSION NUMBER: 1985:22688 HCAPLUS
DOCUMENT NUMBER: 102:22688
TITLE: Human opsonins to meningococci after vaccination
AUTHOR(S): Halstensen, Alfred; **Haneberg, Bjoern**; Froeholm, L. Oddvar; Lehmann, Vidar; Frasch, Carl E.; Solberg, Claus O.
CORPORATE SOURCE: Med. Dep. B, Univ. Bergen, Norway
SOURCE: Infection and Immunity (1984), 46(3), 673-6
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two groups of volunteers were immunized with either a serogroup A plus C **meningococcal** polysaccharide vaccine or a combined **serogroup B** polysaccharide-serotype 2 protein vaccine. Serum opsonin responses were measured by chemiluminescence of polymorphonuclear leukocytes exposed to opsonized live meningococci. Two of the 6 volunteers immunized with the A plus C vaccine had an increase in serum opsonins to group A **meningococci**, 4 responded to **group C meningococci**, and none to **group B meningococci** of 2 different protein serotypes, as well as to a **group C**-serotype 2 **meningococcal** strain. Although no booster effect was obsd. after a second dose of the combined vaccine, both the polysaccharide and the protein components appear to be able to stimulate an opsonin response.

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14mar03 10:53:36 User219783 Session D1924.1

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S2 9591 NMC OR MENC OR (NM OR MEN OR MENINGOCOCC?? OR MENINGITID?)-(S)((GROUP OR SEROGROUP)(W)C) OR GCM
S3 456 S2 AND (NMB OR MENB OR (NM OR MEN OR MENINGOCOCC?? OR MENINGITID?)(S)((GROUP OR SEROGROUP)(W)B) OR GBM)
S4 466 (MENINGOCOCC?? OR MENINGITID? OR (MEN OR NM)(10N)MENING?)(-S)(B(3N)C)

S9 51 (S3 OR S4) AND (ALUM OR (AL OR ALUMIN???)(W)(OH OR HYDROXIDE) OR ALOH? ? OR ALHYDROGEL? ? OR ALHYDRO(W)GEL? ?)

S11 24 S9 AND (OUTER(W)MEMBRAN?(W)(PROTEIN? ? OR VESICLE? ?) OR OMP? ? OR OMV? ?)
S12 23 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

12/3,AB/1 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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02620075 INSIDE CONFERENCE ITEM ID: CN027292152
Effect of *Aluminium"** *Hydroxide"** and *Meningococcal"** *Serogroup"** *C"** Capsular Polysaccharide on the Immunogenicity and Reactogenicity of a *Group"** *B"** Neisseria *meningitidis"** *Outer"** *Membrane"** *Vesicle"** Vaccine
Rosenqvist, E.; Hoeiby, E. A.; Bjune, G.; Aase, A.
CONFERENCE: Modulation of the immune response to vaccine antigens-Symposium
DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, 1998; VOL 92 P: 323-334
Karger, 1998
ISBN: 3805566409
LANGUAGE: English DOCUMENT TYPE: Conference Papers

CONFERENCE EDITOR(S): Brown, F.; Haaheim, L. R.
CONFERENCE SPONSOR: University of Bergen
International Association of Biological Standardization Task Force on Vaccines
CONFERENCE LOCATION: Bergen, Norway
CONFERENCE DATE: Jun 1996 (199606) (199606)

12/3,AB/2 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15563556 PASCAL No.: 02-0263635
Modulation of the serological response to meningococcal polysaccharides by cytokines
DE LOS ANGELES CORTES-CASTILLO Maria; THORPE R; CORBEL M J
Division of Bacteriology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 3QG, United Kingdom
Journal: Vaccine, 2001, 19 (30) 4194-4203
Language: English
*Meningococcal"** A and *C"** but not *B"** capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with *aluminium"** *hydroxide"** and *outer"** *membrane"** *proteins"** . The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/ +) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

12/3,AB/3 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12922610 References: 32
TITLE: Modulation of the serological response to meningococcal polysaccharides by cytokines
AUTHOR(S): Cortes-Castillo MD; Thorpe R; Corbel MJ (REPRINT)
AUTHOR(S) E-MAIL: mcorbel@nibsc.ac.uk
CORPORATE SOURCE: Natl Inst Biol Stand & Controls, Div Bacteriol, Blanche Lane S Mimms/Potters Bar EN6 3QG/Herts/England/ (REPRINT); Natl Inst Biol Stand & Controls, Div Bacteriol, /Potters Bar EN6 3QG/Herts/England/; Natl Inst Biol Stand & Controls, Div Immunobiol, /Potters Bar EN6 3QG/Herts/England/
PUBLICATION TYPE: JOURNAL

PUBLICATION: VACCINE, 2001, V19, N30 (JUL 20), P4194-4203
GENUINE ARTICLE#: 456NZ
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: *Meningococcal"** A and *C"** but not *B"** capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with *aluminium"** *hydroxide"** and *outer"** *membrane"** *proteins"**. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/ +) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

12/3,AB/4 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07083449 References: 33
TITLE: ANTIBODY STUDIES IN MICE OF OUTER MEMBRANE ANTIGENS FOR USE IN AN IMPROVED *MENINGOCOCCAL"** *B"** AND *C"** VACCINE
AUTHOR(S): MILAGRES LG; BRANDILEONE MCC; SACCHI CT; VIEIRA VSD; ZANELLA RC; FRASCH CE
CORPORATE SOURCE: ADOLFO LUTZ INST,BACTERIOL BRANCH,AV DR ARNALDO,351 CERQUEIRA CESAR/BR-01246902 SAO PAULO//BRAZIL/ (Reprint); US FDA,CTR BIOL EVALUAT & RES/BETHESDA//MD/20892
PUBLICATION: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, 1996, V13, N1 (JAN), P9-17
GENUINE ARTICLE#: TR990
ISSN: 0928-8244
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Since 1988, N. meningitis, B:4:P1.15, ET-5 complex, has been responsible for an epidemic of *meningococcal"** disease in Greater Sao Paulo, Brazil. Despite current trials to develop an effective vaccine against *group"** *B"** *meningococci"**, children less than 2 years old have not been protected. It has been suggested that iron-regulated proteins (IRPs) should be considered as potential antigens for *meningococcal"** vaccines. The vaccines under study consisted of *outer"**-*membrane"** *vesicles"** depleted of lipooligosaccharide from three *serogroup"** *B"** strains and one *serogroup"** *C"** strain, IRPs, *meningococcal"** *group"** *C"** polysaccharide and *aluminum"** *hydroxide"**. Four different protein and C: polysaccharide concentrations were studied. The ELISA and bactericidal results showed a higher antibody response when 2

injections of 2.0 mu g doses were administered. Despite higher IgG reactivity against antigen preparations-containing IRPs seen in ELISA, the bactericidal activity was not increased if the target strain was grown in iron-restricted medium, The influence of addition of alkaline-detoxified lipooligosaccharide (dLOS) on immunogenicity of the vaccine was also investigated, and the dLOS provided for a functionally specific antibody response.

12/3,AB/5 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03012234 References: 11
TITLE: IMMUNIZATION AGAINST *SEROGROUP"**-*B"** *MENINGOCOCCI"** - OPSONIN RESPONSE IN VACCINEES AS MEASURED BY CHEMILUMINESCENCE
AUTHOR(S): LEHMANN AK; HALSTENSEN A (Reprint); NAESS A; VOLLSET SE; SJURSEN H; BJUNE G
CORPORATE SOURCE: UNIV BERGEN,HAUKELAND SYKEHUS,DEPT MED/N-5021 BERGEN//NORWAY/ (Reprint); UNIV BERGEN,HAUKELAND SYKEHUS,DEPT MED/N-5021 BERGEN//NORWAY/; UNIV BERGEN,MED INFORMAT & STAT SECT/N-5014 BERGEN//NORWAY/; NATL INST PUBL HLTH/OSLO 1//NORWAY/
PUBLICATION: APMIS, 1991, V99, N8 (AUG), P769-772
GENUINE ARTICLE#: FZ253
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: One hundred and thirteen healthy volunteers were immunized twice (six weeks apart) with four different doses (12.5, 25, 50 and 100-mu-g, measured as protein content) of an *outer"** *membrane"** *vesicle"** vaccine from a *serogroup"** *B"** *meningococcal"** strain (44/76, B:15:P1.16) complexed to *serogroup"** *C"** *meningococcal"** polysaccharide and/or *Al"**(*OH"**)3 i.e. 12 different vaccines. Serum opsonic activity against the *serogroup"** *B"** strain was measured using a chemiluminescence method. A significant rise in serum opsonic activity was demonstrated in 84 volunteers (74%) six weeks after the first injection and in 97 (86%) six weeks after the second. All vaccinees with low preimmunization values (< 25 mVs) experienced a significant increase in opsonic activity. A dose-related response was most evident for the vaccines containing adjuvant, and these vaccines were associated with a maximum response six weeks after the second injection, while the vaccines without *Al"**(*OH"**)3 induced a peak response six weeks after the first injection. The postimmunization opsonic activity was similar to that found in convalescent sera, indicating that the vaccines may protect against *serogroup"** *B"** *meningococcal"** disease.

12/3,AB/6 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00935584
NEISSERIA MENINGITIDIS SEROGROUP B GLYCOCONJUGATES AND METHODS OF USING THE SAME
NEISSERIA MENINGITIDIS SEROGRUPPE B GLYKOKONJUGATE UND VERFAHREN ZU DEREN VERWENDUNG
GLYCOCONJUGUES DU GROUPE SEROLOGIQUE B DE NEISSERIA MENINGITIDIS ET PROCEDES POUR LEUR UTILISATION
PATENT ASSIGNEE:

CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (Proprietor designated states: all)
INVENTOR:
SEID, Robert, C., 737 Peru Street, San Francisco, CA 94112, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 939647 A1 990908 (Basic)
EP 939647 B1 011114
WO 9808543 980305
APPLICATION (CC, No, Date): EP 97936364 970804; WO 97US13609 970804
PRIORITY (CC, No, Date): US 24454 P 960827
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/385
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200146	1132
CLAIMS B	(German)	200146	1071
CLAIMS B	(French)	200146	1338
SPEC B	(English)	200146	9020
Total word count - document A			0
Total word count - document B			12561
Total word count - documents A + B			12561

12/3,AB/7 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00854171
TRANSFERRIN RECEPTOR PROTEIN OF MORAXELLA
TRANSFERRINREZEPTOR PROTEIN AUS MORAXELLA
RECEPTEUR DE TRANSFERRINE CONSTITUE D'UNE PROTEINE DE MORAXELLA
PATENT ASSIGNEE:
Aventis Pasteur Limited, (3092160), 1755 Steeles Avenue West, Toronto, Ontario M2R 3T4, (CA), (Proprietor designated states: all)
INVENTOR:
YANG, Yan-Ping, Apartment 709 120 Torresdale Avenue, Willowdale, Ontario M2R 3N7, (CA)
MYERS, Lisa, E., 187 Elizabeth Street, Guelph, Ontario N1E 2X5, (CA)
HARKNESS, Robin, E., Apartment 1706 640 Sheppard Avenue East, Willowdale, Ontario M2K 1B8, (CA)
KLEIN, Michel, H., 16 Munro Boulevard, Willowdale, Ontario M2P 1B9, (CA)
LEGAL REPRESENTATIVE:
Smart, Peter John (43071), W.H. BECK, GREENER & CO 7 Stone Buildings Lincoln's Inn, London WC2A 3SZ, (GB)
PATENT (CC, No, Kind, Date): EP 866803 A1 980930 (Basic)
EP 866803 B1 021218
WO 97013785 970417
APPLICATION (CC, No, Date): EP 96933285 961011; WO 96CA684 961011
PRIORITY (CC, No, Date): US 540753 951011
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-014/22; C07K-016/12; A61K-039/095;

A61K-039/116; A61K-039/39; G01N-033/569; A61K-047/48; A61K-009/16;
A61K-009/127; A61K-009/00; A61K-009/48
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200251	1157
CLAIMS B	(German)	200251	1197
CLAIMS B	(French)	200251	1254
SPEC B	(English)	200251	8424
Total word count - document A			0
Total word count - document B			12032
Total word count - documents A + B			12032

12/3,AB/8 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00804486
Neisseria meningitidis capsular polysaccharide conjugates
Konjugate von Neisseria Meningitidis Kapselpolysacchariden
Composes conjugues a partir de polysaccharides capsulaires de Neisseria meningitidis
PATENT ASSIGNEE:
CONNAUGHT LABORATORIES LIMITED, (267451), 1755 Steeles Avenue West, Willowdale Ontario M2R 3T4, (CA), (applicant designated states: BE;DE;FR;GB;IT)
INVENTOR:
Kandil, Ali, 245 Park Home Avenue, Willowdale, Ontario M2R 1A1, (CA)
Klein, Michel H., 16 Munro Boulevard, Willowdale, Ontario M2P 1B9, (CA)
Chong, Pele, 32 Estoril Street, Richmond Hill, Ontario L4C 0E6, (CA)
LEGAL REPRESENTATIVE:
Smart, Peter John (43071), W.H. BECK, GREENER & CO 7 Stone Buildings Lincoln's Inn, London WC2A 3SZ, (GB)
PATENT (CC, No, Kind, Date): EP 747063 A2 961211 (Basic)
EP 747063 A3 990324
APPLICATION (CC, No, Date): EP 96304311 960607;
PRIORITY (CC, No, Date): US 474392 950607
DESIGNATED STATES: BE; DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-039/095;

ABSTRACT EP 747063 A2
Capsular polysaccharides containing multiple sialic acid residues, particularly the *Group"** *B"** polysaccharide of Neisseria *meningitidis"**, are modified by chemical reaction to randomly introduce pendant reactive residues of heterobifunctional linker molecules to the polysaccharide backbone. The capsular polysaccharide is deacetylated and the heterobifunctional linker molecule is reacted with the deacetylated material and any residual amino groups are blocked by reaction with alkyl acid anhydride. The introduction of the linker molecules to the polysaccharide chain between the termini enables the polysaccharide to be linked to a carrier molecule, such as a protein, to enhance the immunogenicity of the polysaccharide. The conjugate molecule may be formulated as an immunogenic composition for raising antibodies in a host to the polysaccharide.
ABSTRACT WORD COUNT: 138

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	718
SPEC A	(English)	EPAB96	6289
Total word count - document A			7007
Total word count - document B			0
Total word count - documents A + B			7007

12/3,AB/9 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00787514
Transferrin-binding protein 1 (Tbp1) gene of Actinobacillus pleuropneumoniae, its use in vaccines for pleuropneumonia and as diagnostic reagents
Gen fur dem Tranferrin bindende Protein (Tbp1) aus Actinobacillus pleuropneumoniae, dessen Verwendung in Impfstoffen und als diagnostische Reagenz
Gene de la proteine de liaison de transferrine (Tbp1) d'Actinobacillus pleuropneumoniae, son utilisation dans des vaccins et comme agent diagnostique
PATENT ASSIGNEE:
LABORATORIOS HIPRA, S.A., (1902850), Avenida La Selva s/n, E-17170 Amer (Girona), (ES), (applicant designated states: AT;BE;DE;DK;FR;GB;GR;IE;IT;NL;PT;SE)
INVENTOR:
Daban, Montserrat, Mare de Deu de Montserrat Street No. 263, 08041 Barcelona, (ES)
Espuna, Enric, Av. Paraguay No. 9, 17800 Olot (Girona), (ES)
Medrano, Andres, Av. Can Serra No. X-51, 08906 Hospitalet de Llobregat(Barcelona), (ES)
Querol, Enrique, Vallmajor Street No. 35, 08021 Barcelona, (ES)
LEGAL REPRESENTATIVE:
Claeys, Pierre et al (171), GEVERS Patents, Brussels Airport Business Park, Holidaystraat 5, 1831 Diegem, (BE)
PATENT (CC, No, Kind, Date): EP 733708 A2 960925 (Basic)
EP 733708 A3 970115
APPLICATION (CC, No, Date): EP 96870033 960321;
PRIORITY (CC, No, Date): ES 95592 950324
DESIGNATED STATES: AT; BE; DE; DK; FR; GB; GR; IE; IT; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; C07K-014/285; A61K-039/102; C07K-016/12; G01N-033/569;

ABSTRACT EP 733708 A2
The present invention relates to the gene of transferrin-binding protein 1 (Tbp1) of Actinobacillus pleuropneumoniae, its use to prepare products for vaccination against porcine pleuropneumonia or as diagnostic reagents. The invention also relates to the use of Tbp1 or fragments thereof to produce monoclonal or polyclonal antibodies to be used as diagnostic reagents. The invention also relates to the use of Tbp1 or fragments thereof, alone or combined to other virulence factors of the pathogen, as vaccination products against porcine pleuropneumonia.
ABSTRACT WORD COUNT: 94

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	619
SPEC A	(English)	EPAB96	5159
Total word count - document A			5778
Total word count - document B			0
Total word count - documents A + B			5778

12/3,AB/10 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00542934
Process for converting lipid-containing polysaccharide into lipid-free polysaccharide
Verfahren zum Umwandeln von lipid-haltigen Bakterienkapseln Polysaccharide zu lipid-freien Polysacchariden
Procede pour convertir des polysaccharides bacteriens capsulaires contenant des lipides en des polysaccharides exempts de lipides
PATENT ASSIGNEE:
Merck & Co., Inc., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;PT;SE)
INVENTOR:
Lee, Ann L., 600 Columbia Avenue, Lansdale, PA 19446, (US)
Sitrin, Robert D., 237 Emerson Drive, Lafayette Hill, PA 19444, (US)
Manger, Walter E., 106 Green Bank Way, Harleysville, PA 19438, (US)
Rienstra, Mark S., 405 Bonnie Lane, Lansdale, PA 19446, (US)
LEGAL REPRESENTATIVE:
Barrett-Major, Julie Diane et al (50911), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 528635 A1 930224 (Basic)
EP 528635 B1 990224
APPLICATION (CC, No, Date): EP 92307395 920812;
PRIORITY (CC, No, Date): US 746523 910816; US 909346 920713
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12P-019/04;

ABSTRACT EP 528635 A1
A process for converting lipid-containing bacterial capsular polysaccharide, such as lipo-polyribosyl ribitol phosphate, lipo-PRP, into lipid-free, endotoxin-free polysaccharide, such as polyribosyl ribitol phosphate, PRP, by solubilizing polysaccharide-containing powder derived from culture media of bacteria, such as Haemophilus influenzae type b, cleaving covalently bound fatty acids from the polysaccharide, and removing the lipids, and endotoxin. (see image in original document)
ABSTRACT WORD COUNT: 61

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9907	786
CLAIMS B	(German)	9907	804

CLAIMS B	(French)	9907	885
SPEC B	(English)	9907	11307
Total word count - document A			0
Total word count - document B			13782
Total word count - documents A + B			13782

12/3,AB/11 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00536407
Pneumococcal polysaccharide conjugate vaccine
Imfpstoff, enthaltend ein Pneumokokkenpolysaccharid-Konjugat
Vaccin a base de conjugue de polysaccharide de pneumocoque
PATENT ASSIGNEE:
Merck & Co., Inc., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
INVENTOR:
Kniskern, Peter J., 841 Patterson Drive, Lansdale, PA 19446, (US)
Ip, Charlotte C., 1665 Chadwyck Place, Blue Bell, PA 19422, (US)
Hagopian, Arpi, 771 Hartley Drive, Lansdale, PA 19446, (US)
Hennessey Jr., John P., 114 Fox Hollow Road, Dublin, PA 18917, (US)
Miller, William J., 232 Old Church Road, North Wales, PA 19454, (US)
Kubek, Dennis J., 76 Carolina Avenue, Salem, West Virginia 26426, (US)
Burke, Pamela D., 862 Yorktown Street, Landsdale, PA 19446, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, NJ 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren, NJ 07059, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 497525 A2 920805 (Basic)
EP 497525 A3 930310
EP 497525 B1 980819
APPLICATION (CC, No, Date): EP 92300655 920127;
PRIORITY (CC, No, Date): US 646570 910128; US 807942 911219
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/09; A61K-039/095; A61K-039/295; A61K-039/02; A61K-047/48;

ABSTRACT EP 497525 A2
A novel conjugate vaccine comprising partially hydrolyzed, highly purified, capsular polysaccharide (Ps) from Streptococcus pneumoniae bacteria (pneumococci, Pn) linked to an immunogenic carrier protein, is produced by a new process. The conjugate is useful in the prevention of pneumococcal infections. Vaccines comprising a mixture of from one to ten different pneumococcal polysaccharide-immunogenic protein (Pn-Ps-PRO) conjugates induce broadly protective recipient immune responses against the cognate pathogens from which the polysaccharide components are derived. Young children and infants younger than 2 years old, normally unable to mount a protective immune response to the Pn-Ps alone, exhibit protective immune responses upon vaccination with these Pn-Ps-PRO conjugates.
ABSTRACT WORD COUNT: 105

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9834	1182
CLAIMS B	(German)	9834	1225
CLAIMS B	(French)	9834	1373
SPEC B	(English)	9834	25880
Total word count - document A			0
Total word count - document B			29660
Total word count - documents A + B			29660

12/3,AB/12 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00533711
Conjugates of the class II protein of the outer membrane of neisseria meningitidis and of HIV-1 related peptides.
Konjugate des Klasse-II-Proteins der ausseren Membran von Neisseria Meningitidis mit HIV-1-verwandten Peptiden.
Conjugues de la proteine classe II de la membrane exterieure de neisseria meningitidis et de peptides associes a HIV-1.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;NL)
INVENTOR:
Emini, A., 6 Faggs Manor Lane, Paoli, PA 19301, (US)
Liu, Margaret A., 4 Cushman Road, Rosemont, PA 19190, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, NJ 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren, NJ 07059, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 519554 A1 921223 (Basic)
APPLICATION (CC, No, Date): EP 92201693 920611;
PRIORITY (CC, No, Date): US 715273 910619
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: C07K-017/06; C07K-003/28; A61K-039/385; A61K-039/21;

ABSTRACT EP 519554 A1
The Class II major immuno-enhancing protein (MIEP) of Neisseria meningitidis, purified directly from the outer membrane of Neisseria meningitidis, or obtained through recombinant cloning and expression of DNA encoding the MIEP of Neisseria meningitidis, has immunologic carrier as well as immunologic enhancement and mitogenic properties. Conjugates of this protein and HIV-1 related peptides are useful for the induction of mammalian immune responses directed against the peptides, against HIV-1 strains, and for the neutralization of HIV-1 and prevention of HIV-I related diseases.
ABSTRACT WORD COUNT: 83

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1279
SPEC A	(English)	EPABF1	17403

Total word count - document A 18682
Total word count - document B 0
Total word count - documents A + B 18682

12/3,AB/13 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00508048
IMPROVED VACCINE COMPOSITIONS
VERBESSERTE VAKZINZUSAMMENSETZUNG
VACCIN AMELIORE
PATENT ASSIGNEE:
NORTH AMERICAN VACCINE, INC., (1439710), 10900 Hamon Street, Montreal, Quebec H3M 3A2, (CA), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
PENNEY, Christopher, L., 20 Allenbrooke, Dollard des Ormeaux, Quebec H9A 2S5, (CA)
MICHON, Francis, 429 Nelson Street, Ottawa, Ontario K1N 7S6, (CA)
JENNINGS, Harold, J., 2049 Woodglen Crescent, Gloucester, Ontario K1J 6G6, (CA)
LEGAL REPRESENTATIVE:
Laufhutte, Dieter, Dr.-Ing. et al (61841), Lorenz-Seidler-Gossel Widenmayerstrasse 23, D-80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 549617 A1 930707 (Basic)
EP 549617 B1 960327
WO 9204915 920402
APPLICATION (CC, No, Date): EP 91915418 910912; WO 91CA326 910912
PRIORITY (CC, No, Date): US 583372 900917
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/095; A61K-047/48;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	667
CLAIMS B	(German)	EPAB96	576
CLAIMS B	(French)	EPAB96	736
SPEC B	(English)	EPAB96	6136

Total word count - document A 0
Total word count - document B 8115
Total word count - documents A + B 8115

12/3,AB/14 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00498481
IMPROVED MENINGOCOCCAL POLYSACCHARIDE CONJUGATE VACCINE.
VERBESSERTES MENINGOKOKKALE POLYSACCHARIDKONJUGATVAKZIN.
VACCIN CONJUGUE AMELIORE A BASE DE POLYSACCHARIDE DE MENINGOCOQUE.
PATENT ASSIGNEE:
NATIONAL RESEARCH COUNCIL OF CANADA, (487624), Montreal Road, Ottawa Ontario K1A OR6, (CA), (applicant designated states:

AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
JENNINGS, Harold, J., 2049 Woodglen Crescent, Gloucester, ON, K1J 6G6, (CA)
MICHON, Francis, 128 Keefer Street, Ottawa, ON, K1M 1T5, (CA)
LEGAL REPRESENTATIVE:
Laufhutte, Dieter, Dr.-Ing. et al (61841), Lorenz-Seidler-Gossel Widenmayerstrasse 23, D-80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 504202 A1 920923 (Basic)
EP 504202 B1 950503
WO 9108772 910627
APPLICATION (CC, No, Date): EP 91900142 901213; WO 90CA437 901213
PRIORITY (CC, No, Date): US 448195 891214
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/108; A61K-039/385;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	535
CLAIMS B	(German)	EPAB95	471
CLAIMS B	(French)	EPAB95	607
SPEC B	(English)	EPAB95	4342
Total word count - document A			0
Total word count - document B			5955
Total word count - documents A + B			5955

12/3,AB/15 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00485895
The class II protein of the outer membrane of neisseria meningitidis.
Klasse-II-Protein der ausseren Membran von Neisseria meningitidis und dasselbe enthaltende Impfstoffe.
Classe II de la membrane exterieure de Neisseria meningitidis et raccins la contenant.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Oliff, Allen I., 1412 Florence Drive, Gwynedd Valley, PA 19437, (US)
Liu, Margaret A., 4 Cushman Road, Rosemont, PA 19190, (US)
Friedman, Arther, 121 Froghollow Road, Churchville, PA 18966, (US)
Tai, Joseph Y., 1370 Cinnamon Drive, Fort Washington, PA 19034, (US)
Donnelly, John J., 1505 Briarwood Road, Havertown, PA 19083, (US)
Jones, Deborah D., 1126 Canterbury Drive, Lansdale, PA 19446, (US)
Montgomery, Donna L., 9 Hickory Lane, Chalfont, PA 18914, (US)
Lowe, Robert S., 232 Maple Avenue, Harleysville, PA 19438, (US)
LEGAL REPRESENTATIVE:
Barrett-Major, Julie Diane et al (50911), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 467714 A1 920122 (Basic)
APPLICATION (CC, No, Date): EP 91306618 910719;

PRIORITY (CC, No, Date): US 555329 900719; US 555204 900719; US 555978 900719; US 639457 910110; US 715274 910619
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-013/00; C07K-003/28; C12N-015/09; A61K-039/39; A61K-039/095;

ABSTRACT EP 467714 A1
The Class II major immuno-enhancing protein (MIEP) of Neisseria meningitidis, purified directly from the outer membrane of Neisseria meningitidis, or obtained through recombinant cloning and expression of DNA encoding the MIEP of Neisseria meningitidis, has immunologic carrier as well as immunologic enhancement and mitogenic properties.
ABSTRACT WORD COUNT: 47

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1309
SPEC A	(English)	EPABF1	25077
Total word count - document A			26386
Total word count - document B			0
Total word count - documents A + B			26386

12/3,AB/16 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00485875
Coconjugate vaccines comprising immunogenic protein, HIV related peptides, and anionic moieties.
Impfstoffkonjugatkomplex, das ein immunogenes Protein, HIV-relatierte Peptide und anionischen Gruppen enthalt.
Vaccin comprenant un co-conjugue d'une proteine immunogenique, de peptides lies au HIV et de groupements anioniques.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Leanza, William J., 20 Rutherford Road, Berkeley Heights, NJ 07922, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, NJ 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren, NJ 07059, (US)
Emini, Emilio A., 6 Faggs Manor Lane, Paoli, PA 19301, (US)
LEGAL REPRESENTATIVE:
Barrett-Major, Julie Diane et al (50911), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 467700 A2 920122 (Basic)
EP 467700 A3 930310
APPLICATION (CC, No, Date): EP 91306598 910719;
PRIORITY (CC, No, Date): US 555966 900719; US 715276 910619; US 555339 900719; US 715278 910619
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-007/06; C07K-007/08; C07K-007/54; C07K-015/04; A61K-039/21;

ABSTRACT EP 467700 A2

A novel coconjugate comprising an immunogenic protein or protein complex having a first set of covalent linkages to low molecular weight moieties, -a(sup -), which have an anionic or polyanionic character at physiological pH, and a second set of covalent linkages to peptides comprising Human Immunodeficiency Virus (HIV) Principal Neutralizing Determinants (PNDs), or peptides immunologically equivalent therewith, is useful for inducing anti-peptide immune responses in mammals, for inducing HIV-neutralizing antibodies in mammals, for formulating vaccines to prevent HIV infection or disease, including the Acquired Immune Deficiency Syndrome (AIDS), or for treating humans afflicted with HIV infection or disease.

ABSTRACT WORD COUNT: 100

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	3235
SPEC A	(English)	EPABF1	17206
Total word count - document A			20441
Total word count - document B			0
Total word count - documents A + B			20441

12/3,AB/17 (Item 12 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

00478178

Nucleotide sequence coding for an *outer"** *membrane"** *protein"** from Neisseria meningitidis and use of said protein in vaccine preparations

Nukleotidsequenz, die fur ein Aussenmembran-Protein von Neisseria meningitidis kodiert und Verwendung dieses Proteins zur Herstellung von Impfstoffen

Sequence nucleotidique codant pour une proteine de la membrane externe de Neisseria meningitidis, et utilisation de cette proteine dans la preparation de vaccin

PATENT ASSIGNEE:

CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA, (1256830), 31 Street, '/156 & 190, Cubanacan Playa, Havana, (CU), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:

Rodriguez, Ricardo Silva, Calle 15 No. 4209, entre 42 y 44, Playa, La Habana, (CU)

Houssein Sosa, Manuel Selman, Paseo No. 126, entre 5ta y Calzada, Vedado, La Habana, (CU)

Nieto, Gerardo Guillen, Linea No.6, Apto 4, entre N y O, Vedado, La Habana, (CU)

Herrera Martinez, Luis S. Centro Ingenieria, Genetica y Biotecnoligia 31 Str., '/156 & 190, Cubanacan. Playa Havana, (CU)

Fernandez Maso, Julio RaUl, Calle 26 No.873 1-2,Apto 3, entre Conill y45,Nuevo, La Habana, (CU)

Novoa Perez, Lidia Ines, Calle 184 No.3112, entre 31 y 33, Apto 49, Playa , La Habana, (CU)

Grillo, Juan Morales, Compostela No.653, Apto 1, entre Luz y Acosta, Habana Vieja, La Habana, (CU)

Morera Cordova, Vivian, Calle 184 No.3112, entre 31 y 33, Apto 39, Playa, La Habana, (CU)

Gonzalez Blanco, Sonia, Calle 184 No.3112, entre 31 y 33, Apto 42, Playa, La Habana, (CU)

Santos, Beatriz Tamargo, Calle 202 No.29302, entre 293y295, Reparto Calixto, Sanchez, Boyeros, La Habana, (CU)
del Valle Rosales, JesUs Augusto, D'Strampes N.351, entre San Mariano y Vista Alegre, La Vibora, La Habana, (CU)
Menendez, Evelin Caballero, Calle 7 No.214, entre 2 y 4, Cayo de la Rosa, Bauta, La Habana, (CU)
Alvarez Acosta, Anabel, Calle 184 No.3112, entre 31 y 33, Apto 1, Playa, La Habana, (CU)
Couzeau Rodriguez, Edelgis, Calle 184 No.3112, entre 31 y 33, Apto 20, Playa, La Habana, (CU)
Cruz Leon, Silian, Ave 47 No.11812, entre 118 y 120, Marianao, La Habana, (CU)
Musacchio Lasa, Alexis, Calle 128 No.7117, entre 71 y 73, Mariel, La Habana, (CU)

LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, 2587 BN 's-Gravenhage, (NL)

PATENT (CC, No, Kind, Date): EP 474313 A2 920311 (Basic)
EP 474313 A3 930224
EP 474313 B1 970423

APPLICATION (CC, No, Date): EP 91202291 910906;
PRIORITY (CC, No, Date): CU 14590 900907
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; A61K-039/095; C12P-021/08; C12N-015/62; C12N-015/53; C12N-015/54; C12N-001/21; C12N-001/21; C12R-001/19

ABSTRACT EP 474313 A2
The present invention is concerned with a method for the isolation of a nucleotide sequence which codes for a protein having a molecular weight of about 64 000 daltons, which is located on the outer membrane of N. meningitidis, as well as with the recombinant DNA obtained therefrom, which is used for the transformation of a host microorganism. The technical object pursued with the invention is the identification of a nucleotide sequence coding for a highly conserved and common protein for the majority of pathogenic Neisseria strains, the production of this protein with a high level of purity and in commercially useful amounts using the recombinant way, so that it can be used in diagnostic methods and vaccine preparations with a broad immunoprotection spectrum. (see image in original document)
ABSTRACT WORD COUNT: 131

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	765
CLAIMS B	(English)	EPAB97	305
CLAIMS B	(German)	EPAB97	313
CLAIMS B	(French)	EPAB97	323
SPEC A	(English)	EPABF1	6148
SPEC B	(English)	EPAB97	6260
Total word count - document A			6913
Total word count - document B			7201
Total word count - documents A + B			14114

12/3,AB/18 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00465029
Filamentous hemagglutinin of bordetella pertussis as a carrier molecule for conjugate vaccines.
Faser-Hemagglutinin von Bordetella pertussis als Trager fur konjugierten Impfstoff.
Hemagglutinine filamenteuse de Bordetella pertussis a titre de molecules porteuses pour vaccins conjugues.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;NL;SE)
INVENTOR:
Kimura, Alan, 9856 N.W. 52 Terrace, Miami, FL 33178, (US)
Dick, William Edwin JR., 754 Hawthorne Place, Webster, NY, (US)
Cowell, James Leo, 37 Sugarmills Circle, Fairport, NY 14450, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 471177 A2 920219 (Basic)
EP 471177 A3 930224
EP 471177 B1 951004
APPLICATION (CC, No, Date): EP 91110919 910702;
PRIORITY (CC, No, Date): US 565161 900813
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/10; A61K-039/385;

ABSTRACT EP 471177 A2
This invention pertains to immunogenic conjugates comprising an antigen bound to a filamentous hemagglutinin of Bordetella pertussis and a method of eliciting an immune response against an antigen comprising administering such an immunogenic conjugate with a pharmaceutically acceptable vehicle to a vertebrate host.
ABSTRACT WORD COUNT: 45

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	232
CLAIMS B	(English)	EPAB95	232
CLAIMS B	(German)	EPAB95	248
CLAIMS B	(French)	EPAB95	257
SPEC A	(English)	EPABF1	2515
SPEC B	(English)	EPAB95	2436
Total word count - document A			2747
Total word count - document B			3173
Total word count - documents A + B			5920

12/3,AB/19 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00450306
STABLE VACCINE COMPOSITIONS CONTAINING INTERLEUKINS.
STABILE INTERLEUKINE ENTHALTENDE IMPFSTOFFZUSAMMENSETZUNGEN.
COMPOSITIONS DE VACCIN STABLE CONTENANT DES INTERLEUKINES.

PATENT ASSIGNEE:
PRAXIS BIOLOGICS, INC., (693520), 300 East River Road, Rochester New York 14623, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
PILLAI, Subramonia, 286 Vollmer Parkway, Rochester, NY 14623, (US)
BIXLER, Garvin, 610 East Mountain Road, Knoxville, MD 21758, (US)
LEGAL REPRESENTATIVE:
Allam, Peter Clerk et al (27601), LLOYD WISE, TREGEAR & CO. Norman House 105-109 Strand, London WC2R 0AE, (GB)
PATENT (CC, No, Kind, Date): EP 482076 A1 920429 (Basic)
EP 482076 B1 950426
WO 9101143 910207
APPLICATION (CC, No, Date): EP 90911344 900716; WO 90US3982 900716
PRIORITY (CC, No, Date): US 379742 890714
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	455
CLAIMS B	(German)	EPAB95	440
CLAIMS B	(French)	EPAB95	508
SPEC B	(English)	EPAB95	3033
Total word count - document A			0
Total word count - document B			4436
Total word count - documents A + B			4436

12/3,AB/20 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00443912
MENINGOCOCCAL CLASS 1 *OUTER"**-*MEMBRANE"** *PROTEIN"** VACCINE
MENINGOCOCCALES KLASSE I-AUSSENMEMBRANPROTEIN-VAKZIN
VACCIN MENINGOCOQUE DE LA PROTEINE DE LA MEMBRANE EXTERNE DE LA CLASSE 1
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212595), One Portland Square, Portland, Maine 04101, (US), (Proprietor designated states: all)
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LEGAL REPRESENTATIVE:
Roques, Sarah Elizabeth et al (79543), J.A. Kemp & Co. 14 South Square

Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 449958 A1 911009 (Basic)
EP 449958 B1 950322
EP 449958 B2 021113
WO 90006696 900628
APPLICATION (CC, No, Date): EP 90901397 891219; WO 89US5678 891219
PRIORITY (CC, No, Date): NL 883111 881219; NL 8936 890106; NL 891612 890626
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; C07K-014/22; C07K-007/04; A61K-039/39; A61K-039/385; C12N-015/31; C12N-015/62; C12N-15:31; C12R-1:36
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200246	2221
CLAIMS B	(German)	200246	2207
CLAIMS B	(French)	200246	2873
SPEC B	(English)	200246	14431
Total word count - document A			0
Total word count - document B			21732
Total word count - documents A + B			21732

12/3,AB/21 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00401822
Conjugate immunogen for aids.
Immunogen-Konjugat gegen Aids.
Conjuges immunogenes contre le Sida.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
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Scolnick, Edward M., 811 Wickfield Park Drive, Wynnewood, PA 19096, (US)
Larson, Vivian M., 362 Park Drive, Harleyville PA 19438, (US)
LEGAL REPRESENTATIVE:
Hesketh, Alan, Dr. et al (31763), European Patent Department Merck & Co., Inc. Terlings Park Eastwick Road, Harlow Essex, CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 402088 A2 901212 (Basic)
EP 402088 A3 910306
APPLICATION (CC, No, Date): EP 90306082 900605;
PRIORITY (CC, No, Date): US 362179 890606; US 362178 890606; US 362177 890606; US 362176 890606
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/21; A61K-039/095;

ABSTRACT EP 402088 A2
A conjugate of the major neutralizing determinant of HIV, covalently linked to Neisseria outer membrane proteosome (*Omp"**), is prepared and found to neutralize HIV after inoculation in monkeys. The conjugate is useful as a vaccine against AIDS or ARC as well as in the treatment of

AIDS or ARC.
ABSTRACT WORD COUNT: 53

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1352
SPEC A	(English)	EPABF1	5883
Total word count - document A			7235
Total word count - document B			0
Total word count - documents A + B			7235

12/3,AB/22 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00384471
T-CELL EPITOPE AS CARRIERS MOLECULE FOR CONJUGATE VACCINES.
T-ZELLEN-EPITOPE ALS TRAGER FUR EINEN KONJUGIERTEN IMPFSTOFF.
EPITOPES DE CELLULES T A TITRE DE MOLECULES PORTEUSES POUR VACCINS CONJUGUES.
PATENT ASSIGNEE:
PRAXIS BIOLOGICS, INC., (693521), 30 Corporate Woods, Rochester New York 14623, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
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PILLAI, Subramonia, 286 Vollmer Parkway, Rochester, NY 14623, (US)
INSEL, Richard, 167 Oakdale Drive, Rochester, NY 14618, (US)
LEGAL REPRESENTATIVE:
Allam, Peter Clerk et al (27601), LLOYD WISE, TREGEAR & CO. Norman House 105-109 Strand, London WC2R 0AE, (GB)
PATENT (CC, No, Kind, Date): EP 399001 A1 901128 (Basic)
EP 399001 B1 940727
WO 8906974 890810
APPLICATION (CC, No, Date): EP 89908669 890131; WO 89US388 890131
PRIORITY (CC, No, Date): US 150688 880201
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; C07K-015/04; A61K-039/155;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	747
CLAIMS B	(German)	EPBBF1	655
CLAIMS B	(French)	EPBBF1	800
SPEC B	(English)	EPBBF1	13397
Total word count - document A			0
Total word count - document B			15599
Total word count - documents A + B			15599

12/3,AB/23 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0044344 DBR Accession No.: 86-02192 PATENT
Vaccine against Neisseria meningitidis gp. B infection - containing a single serotype 2b antigen
PATENT ASSIGNEE: U.S.Dept.Health-Human-Serv. 1985
PATENT NUMBER: US 6729206 PATENT DATE: 850924 WPI ACCESSION NO.: 85-316744 (8550)
PRIORITY APPLIC. NO.: US 729206 APPLIC. DATE: 850501
NATIONAL APPLIC. NO.: US 729206 APPLIC. DATE: 850501
LANGUAGE: English
ABSTRACT: A vaccine against Neisseria *meningitidis"** group B serotype 2 is claimed. This contains an *Al"**(*OH"**)3 adjuvant and a single serotype 2b antigen, and is protective against both 2a and 2b *meningococcal"** disease. The nonencapsulated N. *meningitidis"** strain 3006 M2 (ATCC 53044) is used as a starting material and is cultured. The culture supernatant is then concentrated by ultrafiltration and treated with 3 vols of 95% ethanol. The precipitate is dissolved in water and adjusted to 30 mM tris(hydroxymethyl) aminomethane; 2 mM NaEDTA containing 5% Brij 96. The *outer"** *membrane"** *vesicle"** fraction (depleted in lipopolysaccharide) is centrifuged, redissolved in water and protein precipitated with EtOH. This protein can be blended with lactose of gp. *B"** or *C"** polysaccharides (to increase the titer of antibacterial antibodies). 1 ml Doses of the vaccine containing 250-1200 ug protein are then prepared. This vaccine offered protection to humans and stimulated the production of bactericidal antibodies against both the major gp. B *meningococcal"** serotypes. (31pp)

Set	Items	Description
S13	357	AU=(GRANOFF, D? OR GRANOFF D?)
S14	353	AU=(RAFF, H? OR RAFF H?)
S15	86	AU=(AABERGE, I? OR AABERGE I?)
S16	117	AU=(HANEBERG, B? OR HANEBERG B?)
S17	1529	AU=(HOLST, J? OR HOLST J?)
S18	2	S13 AND S14 AND S15 AND S16 AND S17
S19	11	S13 AND (S14 OR S15 OR S16 OR S17)
S20	4	S14 AND (S15 OR S16 OR S17)
S21	14	S15 AND (S16 OR S17)
S22	34	S16 AND S17
S23	20	(S22 OR S13 OR S14 OR S15 OR S16 OR S17) AND (S3 OR S4)
S24	40	(S18 OR S19 OR S20 OR S21 OR S23) NOT S11
S25	22	RD (unique items)

-Author(s)

>>>No matching display code(s) found in file(s): 65, 113

25/3,AB/1 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences

04482660 INSIDE CONFERENCE ITEM ID: CN046894212
Serum bactericidal activity correlates with the vaccine efficacy of outer membrane vesicle vaccines against Neisseria meningitidis serogroup B disease
*Holst, J."**; Feiring, B.; Fuglesang, J. E.; Hoiby, E. A.; Nokleby, H.; *Aaberge, I. S."**; Rosenqvist, E.
CONFERENCE: Vaccines and immunisation-World congress; 3rd
VACCINE -GUILDFORD THEN LONDON THEN OXFORD-, 2003; VOL 21; NO 7-8 P: 734-737
Elsevier, 2003
ISSN: 0264-410X

Searcher : Shears 308-4994

LANGUAGE: English DOCUMENT TYPE: Conference Papers
CONFERENCE EDITOR(S): Kurstak, E.
CONFERENCE SPONSOR: Infections Control World Organization
CONFERENCE LOCATION: Opatija, Croatia 2002; Jun (200206) (200206)
NOTE:
Based on the third world congress on vaccines and immunisation

25/3,AB/2 (Item 2 from file: 65)
DIALOG(R)File 65:Inside Conferences

03897708 INSIDE CONFERENCE ITEM ID: CN040959452
Intranasal group B meningococcal outer membrane vesicle (OMV) vaccines: studies on refinement of the immunization schedule
*Haneberg, B."**; Bakke, H.; Huynh, P. N.; Haugen, I. L.; *Holst, J."**; *Aaberge, I. S."**
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998; 11TH P: 173
Paris, EDK, 1998
ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811) (199811)

25/3,AB/3 (Item 3 from file: 65)
DIALOG(R)File 65:Inside Conferences

03897616 INSIDE CONFERENCE ITEM ID: CN040958538
Patient opsonins against specific meningococcal outer membrane components
Lehmann, A. K.; Guttormsen, H. K.; Wetzler, L. M.; *Aaberge, I. S."**; *Holst, J."**; Gorringe, A. R.; Reddin, K. M.; Smith, I.; Sornes, S.; Halstensen, A.
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998; 11TH P: 65
Paris, EDK, 1998
ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811) (199811)

25/3,AB/4 (Item 4 from file: 65)
DIALOG(R)File 65:Inside Conferences

03897614 INSIDE CONFERENCE ITEM ID: CN040958514
Immunogenicity of a combination of *serogroup"** *C"** conjugate vaccine and an outer membrane-protein based *serogroup"** *B"** vaccine for prevention of Neisseria *meningitidis"** (*Nm"**) disease
*Granoff, D. M."**; *Aaberge, I."**; *Haneberg, B."**; *Holst, J."**; *Raff, H. "**
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998; 11TH P: 61-62
Paris, EDK, 1998

ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811) (199811)

25/3,AB/5 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15627192 PASCAL No.: 02-0331512
Meningococcal outer membrane vesicle vaccine given intranasally can induce immunological memory and booster responses without evidence of tolerance
BAKKE Hilde; LIE Kristian; HAUGEN Inger Lise; KORSVOLD Gro Ellen; HOEIBY E Arne; NAESS Lisbeth Meyer; *HOLST Johan"**; *AABERGE Ingeborg S"**; OFTUNG Fredrik; *HANEBERG Bjoern"**
Department of Vaccinology, National Institute of Public Health, 0403 Oslo , Norway; Department of Microbiology, Institute of Pharmacy, University of Oslo, 0316 Oslo, Norway; Department of Bacteriology, National Institute of Public Health, 0403 Oslo, Norway
Journal: Infection and immunity, 2001, 69 (8) 5010-5015
Language: English
We have studied the ability of outer membrane vesicle (OMV) vaccines from Neisseria meningitidis serogroup B to induce vaccine-specific antibody and spleen cell proliferative responses in mice after being administered intranasally (i.n.) and/or subcutaneously (s.c.). A series of four weekly i.n. doses (25 tag) without adjuvant or a single s.c. dose (2.5 mu g) with aluminum hydroxide was followed 2 months later by secondary i.n. or s.c. immunizations. After i.n. priming, both immunoglobulin G (IgG) antibody responses in serum, measured by enzyme-linked immunosorbent assay, and IgA antibodies in saliva and extracts of feces were significantly boosted by later i.n. immunizations. The IgG antibody responses in serum were also significantly augmented by secondary s.c. immunization after i.n. as well as s.c. priming. Sera from mice immunized i.n. reached the same level of bactericidal activity as after s.c. immunizations. The s.c. immunizations alone, however, had no effect on mucosal IgA antibody responses, but could prime for booster antibody responses in secretions to later i.n. immunizations. The i.n. immunizations also led to marked OMV-specific spleen cell proliferation in vitro. Both serum antibody responses and spleen cell proliferation were higher after i.n. priming and later s.c. immunizations than after s.c. immunizations alone. There was thus no evidence that i.n. priming had induced immunological tolerance within the B- or T-cell system. Our results indicate that a nonproliferating meningococcal OMV vaccine given i.n. can induce immunological memory and that it may be favorably combined with similar vaccines for injections.

25/3,AB/6 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

15603967 PASCAL No.: 02-0308081
Development of vaccines against meningococcal disease
JODAR Luis; FEAVERS Ian M; SALISBURY David; *GRANOFF Dan M"**
World Health Organization, Geneva, Switzerland; National Institute for Biological Standards and Control, Potters Bar, United Kingdom; Department

of Health, London, United States; Children's Hospital Oakland Research Institute, Oakland, CA, United States
Journal: Lancet : (British edition), 2002, 359 (9316) 1499-1508
Language: English

Neisseria *meningitidis"** Is a major cause of bacterial meningitis and sepsis. Polysaccharide-protein conjugate vaccines for prevention of *group"** *C"** disease have been licensed in Europe. Such vaccines for prevention of disease caused by groups A (which is associated with the greatest disease burden worldwide), Y, and W135 are being developed. However, conventional approaches to develop a vaccine for *group"** *B"** strains, which are responsible for most cases in Europe and the USA, have been largely unsuccessful. Capsular polysaccharide-based vaccines can elicit autoantibodies to host polysialic acid, whereas the ability of most non-capsular antigens to elicit broad-based immunity Is limited by their antigenic diversity. Many new membrane proteins have been discovered during analyses of genomic sequencing data. These antigens are highly conserved and, In mice, elicit serum bactericidal antibodies, which are the serological hallmark of protective immunity In man. Therefore, there are many promising new vaccine candidates, and Improved prospects for development of a broadly protective vaccine for *group"** *B"** disease, and for control of all *meningococcal"** disease.

25/3,AB/7 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

14323697 PASCAL No.: 99-0531784
Differences in surface expression of NspA among Neisseria meningitidis group B strains
MOE G R; SIQI TAN; *GRANOFF D M"**
Children's Hospital Oakland Research Institute, Oakland, California 94609, United States
Journal: Infection and immunity, 1999, 67 (11) 5664-5675
Language: English

NspA is a highly conserved membrane protein that is reported to elicit protective antibody responses against Neisseria *meningitidis"** serogroups A, *B"** and *C"** in mice (D. Martin, N. Cadieux, J. Hanel, and B. R. Brodeur, J. Exp. Med. 185:1173-1183, 1997). To investigate the vaccine potential of NspA, we produced mouse anti-recombinant NspA (rNspA) antisera, which were used to evaluate the accessibility of NspA epitopes on the surface of different serogroup B strains by an immunofluorescence flow cytometric assay and by susceptibility to antibody-dependent, complement-mediated bacteriolysis. Among 17 genetically diverse strains tested, 11 (65%) were positive for NspA cell surface epitopes and 6 (35%) were negative. All six negative strains also were resistant to bactericidal activity induced by the anti-rNspA antiserum. In contrast, of the 11 NspA surface-positive strains, 8 (73%; $P < 0.05$) were killed by the antiserum and complement. In infant rats challenged with one of these eight strains, the anti-rNspA antiserum conferred protection against bacteremia, whereas the antiserum failed to protect rats challenged by one of the six NspA cell surface-negative strains. Neither NspA expression nor protein sequence accounted for differences in NspA surface accessibility, since all six negative strains expressed NspA in outer membrane preparations and since their predicted NspA amino acid sequences were 99 to 100% identical to those of three representative positive strains. However, the six NspA cell

surface-negative strains produced, on average, larger amounts of group B polysaccharide than did the 11 positive strains (reciprocal geometric mean titers, 676 and 224, respectively; P < 0.05), which suggests that the capsule may limit the accessibility of NspA surface epitopes. Given these strain differences in NspA surface accessibility, an rNspA-based *meningococcal"** B vaccine may have to be supplemented by additional antigens.

25/3,AB/8 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

14245453 PASCAL No.: 99-0448190
Intranasal immunization with heat-inactivated Streptococcus pneumoniae protects mice against systemic pneumococcal infection
HVALBYE B K R; *AABERGE I S"**; LOEVIK M; *HANEBERG B"**
Department of Vaccinology, National Institute of Public Health, 0403 Oslo , Norway; Department of Environmental Medicine, National Institute of Public Health, 0403 Oslo, Norway
Journal: Infection and immunity, 1999, 67 (9) 4320-4325
Language: English
In order to study the mucosal and serum antibody response to polysaccharide-encapsulated bacteria in mice, a preparation of heat-inactivated Streptococcus pneumoniae type 4 was administered, with and without cholera toxin, at various mucosal sites. It appeared that intranasal immunization of nonanesthesized animals was superior to either oral, gastric, or colonic-rectal antigen delivery with regard to the induction of serum immunoglobulin G (IgG) and IgA, as well as saliva IgA antibodies specific for pneumococci. The marked IgA antibody response in feces after intranasal, but not after oral or gastric, immunization is suggestive of a cellular link between the nasal induction site and the distant mucosal effector sites. Intranasal immunization also induced antibodies in serum and in mucosal secretions against type-specific capsular polysaccharide. IgA and IgG antibody levels in pulmonary lavage fluids correlated well with saliva IgA and serum IgG antibodies, respectively. Antibody determinations in pulmonary secretions may therefore be redundant in some cases, and the number of experimental animals may be reduced accordingly. After intraperitoneal challenge with type 4 pneumococci, mice immunized intranasally were protected against both systemic infection and death, even without the use of cholera toxin as a mucosal adjuvant. Thus, an efficient intranasal vaccine against invasive pneumococcal disease may be based on a very simple formulation with whole killed pneumococci.

25/3,AB/9 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

14120794 PASCAL No.: 99-0316631
Human opsonins induced during meningococcal disease recognize outer membrane proteins PorA and PorB
LEHMANN A K; HALSTENSEN A; *AABERGE I S"**; *HOLST J"**; MICHAELSEN T E;

SOERNES S; WETZLER L M; GUTTORMSEN H K
Medical Department B, University of Bergen, Bergen, Norway; Department of Vaccinology, National Institute of Public Health, Oslo, Norway; Institute of Pharmacy, Department of Pharmacognosy, University of Oslo, Oslo, Norway; Maxwell Laboratory for Infectious Diseases, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, United States; Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States
Journal: Infection and immunity, 1999, 67 (5) 2552-2560
Language: English
Human opsonins directed against specific meningococcal outer membrane structures in sera obtained during meningococcal disease were quantified with a recently developed antigen-specific, opsonin-dependent phagocytosis and oxidative burst assay. Outer membrane vesicles (OMVs) and PorA (class 1) and PorB (class 3) proteins purified from mutants of the same strain (44/76; B:15:P1.7.16) were adsorbed to fluorescent beads, opsonized with acute- and convalescent-phase sera from 40 patients with meningococcal disease, and exposed to human leukocytes. Flow cytometric quantitation of the resulting leukocyte phagocytosis products (PPs) demonstrated that disease-induced serum opsonins recognized meningococcal OMV components and both porins. The PP SUB P SUB o SUB r SUB A and PP SUB P SUB o SUB r SUB B values induced by convalescent-phase sera correlated positively with the PP SUB O SUB M SUB V values. However, the PP SUB P SUB o SUB r SUB B values were higher than the PP SUB P SUB o SUB r SUB A values in convalescent-phase sera (medians (ranges) of 754 (17 to 1,057) and 107 (4 to 458), respectively) ($P < 0.0001$) and correlated positively with higher levels of immunoglobulin G against PorB than against PorA as evaluated by enzyme-linked immunosorbent assay. Extensive individual variations in the anti-OMV and antiporin serum opsonic activities between patients infected by serotypes and serosubtypes homologous and heterologous to the target antigens were observed. Simultaneously measured oxidative burst activity correlated with the opsonophagocytosis, an indication that both of these important steps in the in vitro phagocytic elimination of meningococci are initiated by opsonins directed against OMV components, including PorA and PorB. In conclusion, human patient opsonins against meningococcal OMV components and in particular PorB epitopes were identified by this new method, which might facilitate selection of opsonin-inducing meningococcal antigens for inclusion in future vaccines.

25/3,AB/10 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

12990692 PASCAL No.: 97-0270397
MF59 adjuvant enhances antibody responses of infant baboons immunized with Haemophilus influenzae type b and Neisseria meningitidis group C Oligosaccharide-CRM SUB 1 SUB 9 SUB 7 conjugate vaccine
*GRANOFF D M"**; MCHUGH Y E; *RAFF H V"**; MOKATRIN A S; VAN NEST G A
Chiron Vaccines, Emeryville, California 94608, United States; Children's Hospital Oakland Research Institute, Oakland, California 94609, United States
Journal: Infection and immunity, 1997, 65 (5) 1710-1715
Language: English
The ability of the adjuvant MF59 to enhance the immunogenicity of polysaccharide-protein conjugate vaccines was investigated in infant baboons. MF59 consists of stable droplets (<250 nm) of the metabolizable

oil squalene and two surfactants, polyoxyethylene sorbitan monooleate and sorbitan trioleate, in an oil-in-water emulsion. In humans, MF59 is well tolerated and enhances the immunogenicity of recombinant protein subunit or particle vaccines. Its effect on the immunogenicity of polysaccharide-protein conjugate vaccines is unknown. Baboons 1 to 4 months of age were immunized intramuscularly with Neisseria meningitidis group C and Haemophilus influenzae type b (Hib) oligosaccharide-CRM SUB 1 SUB 9 SUB 7 conjugate vaccines. The lyophilized vaccines were reconstituted with phosphate-buffered saline (PBS), Al(OH) SUB 3 (alum), or MF59. Groups of five animals each were given three injections of the respective formulations, with one injection every 4 weeks. Four weeks after each immunization, the MF59 group had up to 7-fold-higher geometric mean anticapsular-antibody titers than the alum group and 5- to 10-fold-higher N. meningitidis group C bactericidal-antibody titers. Twenty-one weeks after the third immunization, the MF59 group still showed 5- to 10-fold-higher anticapsular-antibody titers. The antibody responses of the animals given the vaccines reconstituted with PBS were low at all times measured. Both the MF59 and alum groups, but not the PBS group, showed booster antibody responses to unconjugated Hib and N. meningitidis group C polysaccharides, results consistent with induction of memory B cells. Thus, MF59 may be useful for accelerating and augmenting immunity to polysaccharide-protein conjugate vaccines in infants.

25/3,AB/11 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal

12865876 PASCAL No.: 97-0124929
Functional assays for evaluation of serogroup B meningococcal structures as mediators of human opsonophagocytosis
LEHMANN A K; HALSTENSEN A; *HOLST J"**; BASSOE C F
Medical Department B, University of Bergen, Haukeland Hospital, N-5021, Bergen, Norway; Department of Vaccinology, National Institute of Public Health, N-0462, Oslo, Norway
Journal: Journal of immunological methods, 1997, 200 (1-2) 55-68
Language: English Summary Language: English

Functional flow cytometry and chemiluminescence (CL) assays have been modified to identify serogroup B *meningococcal"** structures that mediate anti-*meningococcal"** opsonophagocytosis. Serogroup B *meningococcal"** outer membrane vesicles (OMV) were adsorbed to fluorescent latex beads (OMV-beads) and opsonized with acute phase and convalescence sera from patients with serogroup B *meningococcal"** disease. Phagocytosis of these beads by human monocytes and polymorphonuclear leukocytes (non-lymphocytes) was dependent on both antigen exposure on the bead surface and on serum opsonization. OMV-beads opsonized with serum from a patient recovering from *meningococcal"** disease, caused 97% of the non-lymphocytes to phagocytose an average of 15.8 beads per cell with a CL response of 46 550 mVs, whereas opsonized control beads were phagocytosed by 19% of the non-lymphocytes with 1.1 beads per cell and a CL response of 53 mVs. Increased amounts of functional, anti-OMV opsonins were detected during infection, and opsonized OMV-beads elicited phagocyte responses of similar magnitude to those of opsonized whole *meningococci"**. Phagocyte internalization of OMV-beads was confirmed by confocal laser scanning microscopy. We conclude that epitopes on the *meningococcal"** outer

membrane are recognized by anti-*meningococcal"** opsonins in these functional phagocytosis assays, which provide a basis for subsequent evaluation of various purified bacterial components as mediators of human opsonophagocytic responses and hence future vaccine constituents.

25/3,AB/12 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

12110563 PASCAL No.: 95-0340644
Human immunoglobulin M paraproteins cross-reactive with Neisseria meningitidis Group B polysaccharide and fetal brain
AZMI F H; LUCAS A H; SPEIGELBERG H L; *GRANOFF D M"**
Children's hosp. Oakland res. inst., Oakland CA 94609, USA
Journal: Infection and immunity, 1995, 63 (5) 1906-1913
Language: English
Three hundred fifty-nine serum samples from patients with immunoglobulin M (IgM) or IgG monoclonal gammopathies were tested for binding to the capsular polysaccharide (PS) of Neisseria *meningitidis"** group B (MenB PS, poly- alpha (2 rightarrow alpha) -N-acetylneuraminic acid). Of 159 IgM paraproteins, 7 (4.4%) were positive, compared with 0 of 200 IgG paraproteins (P<0.05). Since MenB PS reactivity was limited to the IgM paraproteins, the 1S9 IgM paraproteins were tested by enzyme-linked immunosorbent assay (ELISA) for reactivity with seven other bacterial PSs. None reacted with *meningococcal"** A or *C"**, Haemophilus influenzae type *b"**, or Streptococcus pneumoniae type 3, 6, 14, or 23 PS. The specificity of the MenB PS-reactive antibodies was confirmed by demonstration of binding to N. meningindis group B cells but not to a capsular PS-deficient mutant and by specific inhibition of binding to solid-phase MenB PS by soluble MenB PS in an ELISA. Five of five antibodies tested protected infant rats from bacteremia caused by Escherichia coli K1, an organism with a PS capsule that also is composed of poly- alpha (2 rightarrow 8) -N-acetylneuraminic acid. Each of the seven MenB PS-reactive paraproteins had autoantibody activity as defined by binding to homogenates of calf brain in a radioimmunoassay. For six of the seven antibodies, binding to calf brain was inhibited by the addition of soluble MenB PS. Thus, approximately 4% of human IgM paraproteins have autoantibody activity to poly- alpha (2 rightarrow 8)-N-acetylneuraminic acid, an antigen expressed in fetal brain and cross-reactive with the MenB capsular PS. The reason for this skewing of the IgM paraprotein repertoire toward reactivity with poly-alpha (2 rightarrow 8)-N-acetylneuraminic acid antinic determinants is unknown

25/3,AB/13 (Item 9 from file: 144)
DIALOG(R)File 144:Pascal

11635641 PASCAL No.: 94-0487100
Variable region sequences and idiotypic expression of a protective human immunoglobulin M antibody to capsular polysaccharides of Neisseria meningitidis group B and Escherichia coli K1
AZMI F H; LUCAS A H; *RAFF H V"**; *GRANOFF D M"**
Washington univ. school medicine, Edward Mallinckrodt dep. pediatrics, div. infectious diseases, St. Louis MO, USA

Journal: Infection and immunity, 1994, 62 (5) 1776-1786
Language: English
We determined the heavy (H)- and light (L)-chain variable (V) region nucleotide and translated amino acid sequences of the human immunoglobulin M(kappa) monoclonal antibody (MAb) 5E1, which is specific for the polysacchyride capsule of Escherichia coli K1 and Neisseria meningitidis group B (poly(alpha (2 rightarrow 8)-N-acetylneuraminic acid)) and which is protective in animal models of infection. The 5E1 V SUB L gene is a member of the V SUB H IIIb family and is 97% homologous to the 9.1 germ line gene. The 5E1 V SUB L gene is a member of the kappa I subgroup and is 98% homologous to the germ line gene, 15A, also known as KLO12

25/3,AB/14 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00300067
IDENTIFYING NO.: 5R01AI46464-02 AGENCY CODE: CRISP
CONSERVED NEISSERIA PROTEINS AS VACCINE CANDIDATES
PRINCIPAL INVESTIGATOR: *GRANOFF, DAN M"**
ADDRESS: CHILDREN'S HPTL OAKLAND RES IN 5700 MARTIN LUTHER KING JR WAY OAKLAND, CA 94609
PERFORMING ORG.: CHILDREN'S HOSPITAL OAKLAND, OAKLAND, CALIFORNIA
SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
FY : 2001
SUMMARY: DESCRIPTION: (Adapted from Applicant's Abstract) The long-term objective of this study is to increase our understanding of the use of conserved membrane proteins as components of a vaccine for prevention of Neisseria *meningitidis"** serogroup B (MenB) disease. MenB is a major cause of meningitis and sepsis. Although serum bactericidal antibodies confer protection, to date, conventional approaches to develop a vaccine have been largely unsuccessful. Polysaccharide-based MenB vaccines risk eliciting autoantibodies to host polysialic acid, while the ability of most non-capsular antigens to elicit broad-based immunity is limited by antigenic diversity. We propose to investigate the vaccine potential of three recently discovered conserved Neisserial membrane proteins, designated Neisserial surface proteins (Nsp) A, *B"**, and *C"**. As backup candidates, NspD and NspE are also available. NspA was discovered with a monoclonal antibody, while the other four proteins represent new vaccine candidates that were discovered from analysis of genomic data. All five proteins are highly conserved across pathogenic Neisseria, have epitopes on the surface of the bacteria that are accessible to antibody, and elicit complement-mediated bactericidal antibodies in mice or rabbits. Thus, each of these proteins deserves further investigation as candidate antigens for inclusion in a MenB vaccine. In Aim 1, we will investigate the immunogenicity of each of the recombinant proteins in mice and guinea pigs. Should the recombinant molecules fail to elicit high titers of antibodies that are functionally active against the bacteria, we will attempt to reconstitute conformational epitopes with the use of detergents or liposomes, and explore the use of novel adjuvants suitable for human use. In Aim 2, we will prepare monoclonal antibodies (Mabs) that react with epitopes on the Ns proteins that are important in eliciting protective antibodies. These Mabs will be used for epitope mapping, and for studies of antibody functional activity. In Aim 3, we also will use the 3Iabs to investigate whether there are strain differences in surface accessibility and expression of the different NS proteins, and correlate any differences found with the respective DNA sequences encoding the proteins, or

transcriptional activity of the respective genes. We also will investigate whether surface accessibility of the different Ns proteins varies within a Neisserial strain when propagated in vitro, or in infant rats. In Aim 4, we will test the hypothesis that a vaccine containing more than one Ns protein will elicit broader protective immunity to MenB than a vaccine made from a single protein. These results are directly relevant to evaluating the potential for inclusion or exclusion of each of these novel proteins in a MenB vaccine. The data also may validate the genomic approach for identification of new antigenic targets for vaccine development.

25/3,AB/15 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15399239 Document Delivery Available: 000180212000035 References: 49
TITLE: Age-related disparity in functional activities of human *group"** *C"** serum anticapsular antibodies elicited by *meningococcal"** polysaccharide vaccine
AUTHOR(S): Harris SL; King WJ; Ferris W; *Granoff DA (REPRINT)"**
AUTHOR(S) E-MAIL: dgranoff@chori.org
CORPORATE SOURCE: 5700 Martin Luther King Jr Way, /Oakland//CA/94609 (REPRINT); Childrens Hosp Oakland, Res Inst, /Oakland//CA/94609; Univ Ottawa, Dept Pediat, /Ottawa/ON/Canada/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2003, V71, N1 (JAN), P275-286
GENUINE ARTICLE#: 632EZ
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Serum bactericidal activity confers protection against *meningococcal"** disease, but it is not known whether vaccine-induced anticapsular antibodies that lack bactericidal activity are protective. We developed an infant rat challenge model using a naturally occurring O-acetylated strain of Neisseria *meningitidis"** *group"** *C"** and a strain that was negative for 0 acetylation (OAc). Rats 4 to 7 days of age inoculated intraperitoneally (i.p.) with similar to10(3) CFU of either strain developed >5 X 10(5) CFU/ml of blood obtained 18 h later. Dilutions of preimmunization sera given i.p. 2 h before the bacterial challenge had no effect on bacteremia, whereas *group"** *C"** anticapsular antibody in sera from adults immunized with *meningococcal"** polysaccharide vaccine conferred complete or partial (>99% decrease in CFU per milliliter of blood) protection against the OAc-positive or OAc-negative strain, respectively, at antibody doses as low as 0.04 mug/rat. Anticapsular antibody at doses fivefold higher (0.18 to 0.2 mug/rat) in pooled sera from children immunized at a mean age of 2.6 years failed to protect rats, but antibody at the same or fivefold-lower dose in a serum pool from a group of children immunized at 4 years of age gave complete or partial protection. Protective activity was observed with some serum pools that lacked detectable complement-mediated bactericidal activity (titers < 1:4) and correlated with increasing antibody avidity. Thus, not only does the magnitude of the *group"** *C"** antibody response to *meningococcal"** polysaccharide vaccine increase with increasing age but there are also age-related affects on antibody functional activity such that higher serum concentrations of vaccine-induced antibody are required for protection of immunized children than for immunized adults.

25/3,AB/16 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13265882 References: 43
TITLE: A novel mimetic antigen eliciting protective antibody to Neisseria meningitidis
AUTHOR(S): *Granoff DM (REPRINT)"**; Moe GR; Giuliani MA; Adu-Bobie J; Santini L; Brunelli B; Piccinetti F; Zuno-Mitchell P; Lee SS; Neri P; Bracci L; Lozzi L; Rappuoli R
AUTHOR(S) E-MAIL: dgranoff@chori.org
CORPORATE SOURCE: Childrens Hosp, Oakland Res Inst, 5700 Martin Luther King Jr Way/Oakland//CA/94609 (REPRINT); Childrens Hosp, Oakland Res Inst, /Oakland//CA/94609; Inst Ric Immunobiol, /Siena//Italy/; Univ Siena, Dept Biol Mol, /I-53100 Siena//Italy/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF IMMUNOLOGY, 2001, V167, N11 (DEC 1), P6487-6496
GENUINE ARTICLE#: 494WU
PUBLISHER: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
ISSN: 0022-1767
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Molecular mimetic Ags are of considerable interest as vaccine candidates. Yet there are few examples of mimetic Ags that elicit protective Ab against a pathogen, and the functional activity of anti-mimetic Abs has not been studied in detail. As part of the Neisseria meningitidis serogroup B genome sequencing project, a large number of novel proteins were identified. Herein, we provide evidence that genome-derived Ag 33 (GNA33), a lipoprotein with homology to Escherichia coli murein transglycosylase, elicits protective Ab to meningococci as a result of mimicking an epitope on loop 4 of porin A (PorA) in strains with serosubtype P1.2. Epitope mapping of a bactericidal anti-GNA33 mAb using overlapping peptides shows that the mAb recognizes peptides from GNA33 and PorA that share a QTP sequence that is necessary but not sufficient for binding. By How cytometry, mouse antisera prepared against rGNA33 and the anti-GNA33 mAb bind as well as an anti-PorA P1.2 mAb to the surface of eight of nine N. meningitidis serogroup B strains tested with the P1.2 serosubtype. Anti-GNA33 Abs also are bactericidal for most P1.2 strains and, for susceptible strains, the activity of an anti-GNA33 mAb is similar to that of an anticapsular mAb but less active than an anti-P1.2 mAb. Anti-GNA Abs also confer passive protection against bacteremia in infant rats challenged with P1.2 strains. Thus, GNA33 represents one of the most effective immunogenic mimetics yet described. These results, demonstrate that molecular mimetics have potential as meningococcal vaccine candidates.

25/3,AB/17 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10643424 References: 30
TITLE: Neisseria meningitidis serogroup B outer membrane vesicle vaccine in adults with occupational risk for meningococcal disease
AUTHOR(S): Fischer M; Carlone GM; *Holst J"**; Williams D; Stephens DS; Perkins BA (REPRINT)

AUTHOR(S) E-MAIL: bap4@cdc.gov
CORPORATE SOURCE: 1600 Clifton Rd NE,MS C-09, /Atlanta//GA/30333 (REPRINT); Childrens Hosp & Reg Med Ctr, Dept Pediat, /Seattle//WA/; Natl Ctr Infect Dis, Ctr Dis Control & Prevent, /Atlanta//GA/; Emory Univ, Div Infect Dis, /Atlanta//GA/30322; Natl Inst Publ Hlth, Dept Vaccinol, /N-0462 Oslo//Norway/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 1999, V17, N19 (MAY 14), P2377-2383
GENUINE ARTICLE#: 205BF
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Vaccination provides a safe and effective means of reducing the risk of laboratory-acquired infection due to some Neisseria *meningitidis"** serogroups. However, there is currently no serogroup B *meningococcal"** vaccine licensed for use in the US. We used an investigational N. *meningitidis"** serogroup B outer membrane vesicle (B:15:P1.7,16) vaccine produced by the National Institute of Public Health (NIPH) in Norway to immunize 20 researchers with occupational risk for disease. Three doses of vaccine were administered via intramuscular injection at 8-week intervals. The vaccine produced moderate or severe pain with 19 (33%) of the 58 doses administered. Reactions were similar following first, second and third doses. The number and severity of reactions peaked at 24 h postvaccination and then gradually waned. Of 16 vaccinees with results available from all blood draws, 12 (75%) showed a fourfold or greater rise in serum bactericidal activity (SBA) against the Vaccine type-strain following two doses of vaccine, and 15 (94%) responded after three doses. Geometric mean titers increased by more than sixfold following two doses of vaccine when compared with prevaccination levels, and by more than Ii-fold following a third dose. There was no significant difference between SEA measured using the vaccinee's own complement versus a donor complement source. The NIPH vaccine elicited an excellent bactericidal response against the vaccine type-strain in researchers with an occupational risk for disease. It may be useful for other laboratory personnel who routinely work with *meningococcal"** strains containing similar outer membrane antigens. These findings reconfirm that the NIPH vaccine is immunogenic in adults and support the validity of using properly screened human donor complement in serum bactericidal assays against serogroup *B"** *meningococci"**. (*C"**) 1999 Elsevier Science Ltd. All rights reserved.

25/3,AB/18 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10009037 References: 23
TITLE: Induction of immunologic memory by conjugated vs plain meningococcal C polysaccharide vaccine in toddlers: A randomized controlled trial
AUTHOR(S): MacDonald NE (REPRINT); Halperin SA; Law BJ; Forrest B; Danzig LE; *Granoff DM"**
CORPORATE SOURCE: CHILDRENS HOSP EASTERN ONTARIO,401 SMYTH RD/OTTAWA/ON K1H 8L1/CANADA/ (REPRINT); UNIV OTTAWA,/OTTAWA/ON/CANADA/; DALHOUSIE UNIV,/HALIFAX/NS/CANADA/; UNIV MANITOBA,/WINNIPEG/MB/CANADA/; CHIRON CORP,CHIRON VACCINES/EMERYVILLE//CA/; CHILDRENS HOSP,OAKLAND RES INST/OAKLAND//CA/94609

09/701453

PUBLICATION TYPE: JOURNAL
PUBLICATION: JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 1998, V280, N19 (NOV 18), P1685-1689
GENUINE ARTICLE#: 138PD
PUBLISHER: AMER MEDICAL ASSOC, 515 N STATE ST, CHICAGO, IL 60610
ISSN: 0098-7484
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Context.-*Meningococcal"** polysaccharide vaccines are not used routinely in infants and toddlers, the groups at highest risk of invasive disease, because of poor immunologic responses to the Neisseria *meningitidis"** *serogroup"** *C"** polysaccharide in these age groups. *Meningococcal"** C conjugate vaccines offer the prospect of circumventing this problem.

Objective.-To assess the immunogenicity and the induction of immunologic memory in toddlers by meningococcal C conjugate vaccine.

Design.-A multicenter, randomized, observer-blinded controlled trial.

Setting.-Urban and suburban family medicine or pediatric practices,

Participants.-Two hundred eleven healthy toddlers aged 15 to 23 months.

Intervention.-Two injections at 2 months apart of meningococcal C conjugate (group 1, n = 69), plain meningococcal polysaccharide (group 2, n = 72), or hepatitis B virus vaccine (group 3, n = 70). All toddlers received a follow-up dose of plain meningococcal polysaccharide vaccine 12 months later.

Main Outcome Measures.-IgG meningococcal C anticapsular antibody concentrations determined by enzyme-linked immunosorbent assay and complement-mediated bactericidal antibody.

Results.-In group 1, the magnitude of the IgG response to meningococcal C conjugate vaccine was more than 4-fold higher after dose 1 and more than 10-fold higher after dose 2 compared with meningococcal polysaccharide vaccine (group 2) (P<.001). Higher titers persisted in the meningococcal C conjugate group for at least 12 months (P<.001). Group 1, primed with meningococcal C conjugate, had 25-fold higher IgG responses to the meningococcal polysaccharide 1-year booster dose than the controls who had received hepatitis B virus vaccine initially and were given meningococcal polysaccharide vaccine 1 year later for the first time (P<.001). In contrast, group 2, primed with meningococcal polysaccharide, had a 2-fold lower response to the 1-year booster meningococcal polysaccharide dose than the hepatitis B virus control group (P=.006), Serum bactericidal responses paralleled the enzyme-linked immunosorbent assay responses.

Conclusions.-Immunization of toddlers with meningococcal C conjugate vaccine induces high titers of anticapsular and bactericidal antibody. Furthermore, this vaccine induces immunologic memory to meningococcal C polysaccharide. In contrast, meningococcal polysaccharide vaccine is less immunogenic than the conjugate vaccine and also induces a hyporesponsive state that persists for at least 12 months.

Searcher : Shears 308-4994

09625485 References: 26
TITLE: A modified enzyme-linked immunosorbent assay for measurement of antibody responses to meningococcal C polysaccharide that correlate with bactericidal responses
AUTHOR(S): *Granoff DM (REPRINT)"**; Maslanka SE; Carlone GM; Plikaytis BD; Santos GF; Mokatrin A; *Raff HV"**
CORPORATE SOURCE: CHIRON VACCINES,4560 HORTON ST, R-311/EMERYVILLE//CA/94608 (REPRINT); CHILDRENS HOSP OAKLAND,RES INST/OAKLAND//CA/94609; CTR DIS CONTROL & PREVENT,DIV BACTERIAL & MYCOT DIS/ATLANTA//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 1998, V5, N4 (JUL), P479-485
GENUINE ARTICLE#: ZY123
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 1071-412X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The standardized enzyme-linked immunosorbent assay (ELISA) for measurement of serum immunoglobulin G (IgG) antibody responses to meningococcal C polysaccharide has been modified to employ assay conditions that ensure specificity and favor detection primarily of high-avidity antibodies. The modified and standard assays were used to measure IgG antibody concentrations in sera of toddlers vaccinated with meningococcal polysaccharide vaccine or a meningococcal C conjugate vaccine. The results were compared to the respective complement-mediated bactericidal antibody titers. In sera obtained after one or two doses of vaccine, the correlation coefficients, r, for the results of the standard assay and bactericidal antibody titers were 0.45 and 0.29, compared to 0.85 and 0.87, respectively, for the modified assay. With the standard assay, there were no significant differences between the geometric mean antibody responses of the two vaccine groups. In contrast, with the modified assay, 5- to 20-fold higher postvaccination antibody concentrations were measured in the conjugate than in the polysaccharide group. Importantly, the results of the modified assay, but not the standard ELISA, paralleled the respective geometric mean bactericidal antibody titers. Thus, by employing conditions that favor detection of higher-avidity IgG antibody, the modified ELISA provides results that correlate closely with measurements of antibody functional activity that are thought to be important in protection against meningococcal disease.

25/3,AB/20 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09455000 References: 31
TITLE: Bactericidal monoclonal antibodies that define unique meningococcal B polysaccharide epitopes that do not cross-react with human polysialic acid
AUTHOR(S): *Granoff DM (REPRINT)"**; Bartoloni A; Ricci S; Gallo E; Rosa D; Ravenscroft N; Guarnieri V; Seid RC; Shan A; Usinger WR; Tan SQ; McHugh YE; Moe GR
CORPORATE SOURCE: CHIRON VACCINES,4560 HORTON ST, R-311/EMERYVILLE//CA/94608 (REPRINT); CHIRON VACCINES,/SIENA//ITALY/; CHILDRENS HOSP OAKLAND,RES INST/OAKLAND//CA/94609

PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1998, V160, N10 (MAY 15), P5028-5036
GENUINE ARTICLE#: ZM053
PUBLISHER: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
ISSN: 0022-1767
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The poor immunogenicity of the Neisseria *meningitidis"** *group"** *B"** polysaccharide capsule, a homopolymer of alpha(2-->8) sialic acid, has been attributed to immunologic tolerance induced by prenatal exposure to host polysialyated glycoproteins, Substitution of N-propionyl (N-Pr) for N-acetyl groups on the *meningococcal"** B polysaccharide, and conjugation of the resulting polysaccharide to a protein carrier, have been reported to yield a conjugate vaccine that elicits protective Abs with minimal autoantibody activity. To characterize the protective epitopes on the derivatized polysaccharide, we isolated 30 anti-N-Pr *meningococcal"** B polysaccharide mAbs, These Abs were heterogeneous with respect to complement-mediated bactericidal activity, fine antigenic specificity, and autoantibody activity as defined by binding to the neuroblastoma cell line, CW-134, which expresses long-chain alpha(2-->8)-linked polysialic acid. Eighteen of the Abs could activate complement-mediated bacteriolysis, Seven of these 18 Abs cross-reacted with N-acetyl *meningococcal"** B polysaccharide by ELISA and had strong autoantibody activity, Thus, N-Pr *meningococcal"** B polysaccharide conjugate vaccine has the potential to elicit autoantibodies. However, 7 of the 18 bactericidal mAbs had no detectable autoantibody activity. These Abs may be useful for the identification of molecular mimetics capable of eliciting protective Abs specific to the bacteria, without the risk of evoking autoimmune disease.

25/3,AB/21 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08405378 References: 44
TITLE: MF59 adjuvant enhances antibody responses of infant baboons immunized with Haemophilus influenzae type b and Neisseria meningitidis *group"** *C"** oligosaccharide-CRM197 conjugate vaccine
AUTHOR(S): *Granoff DM (REPRINT)"**; McHugh YE; *Raff HV"**; Mokatrin AS; VanNest GA
CORPORATE SOURCE: CHIRON CORP,VACCINES, 4560 HORTON ST, R-311/EMERYVILLE//CA/94608 (REPRINT); CHILDRENS HOSP,OAKLAND RES INST/OAKLAND//CA/94609
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1997, V65, N5 (MAY), P1710-1715
GENUINE ARTICLE#: WW398
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The ability of the adjuvant MF59 to enhance the immunogenicity of polysaccharide-protein conjugate vaccines was investigated in infant baboons, MF59 consists of stable droplets (<250 *nm"**) of the metabolizable oil squalene and two surfactants, polyoxyethylene sorbitan monooleate and sorbitan trioleate, in an oil-in-water emulsion. In humans,

MF59 is well tolerated and enhances the immunogenicity of recombinant protein subunit or particle vaccines. Its effect on the immunogenicity of polysaccharide-protein conjugate vaccines is unknown. Baboons 1 to 4 months of age were immunized intramuscularly with Neisseria *meningitidis"** *group"** *C"** and Haemophilus influenzae type b (Hib) oligosaccharide-CRM197 conjugate vaccines. The lyophilized vaccines were reconstituted with phosphate-buffered saline (PBS), Al(OH)(3) (alum), or MF59. Groups of five animals each were given three injections of the respective formulations, with one injection every 4 reeks. Four weeks after each immunization, the MF59 group had up to 7-fold-higher geometric mean anticapsular-antibody titers than the alum group and 5- to 10-fold-higher N. *meningitidis"** *group"** *C"** bactericidal-antibody titers. Twenty one weeks after the third immunization, the MF59 group still showed 5- to 10-fold-higher anticapsular-antibody titers, The antibody responses of the animals given the vaccines reconstituted with PBS were low at all times measured, Both the MF59 and alum groups, but not the PBS group, showed booster antibody responses to unconjugated Hib and N. *meningitidis"** *group"** *C"** polysaccharides, results consistent with induction of memory B cells. Thus, MF59 may be useful for accelerating and augmenting immunity to polysaccharide-protein conjugate vaccines in infants.

25/3,AB/22 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01114225
COMBINATION *MENINGITIDIS"** *B"**/*C"** VACCINES
KOMBINIERTE MENINGITIS B/C IMPFSTOFFE
VACCIN MIXTE B/C CONTRE LA MENINGITE
PATENT ASSIGNEE:
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*AABERGE, Ingeborg, S."**, Statens Institutt for Folkehelse, P.O. Box 4404, N-0403 Oslo, (NO)
*HANEBERG, Bjorn"**, Statens Institutt for Folkehelse, P.O. Box 4404, N-0403 Oslo, (NO)
*HOLST, Johan"**, Statens Institutt for Folkehelse, P.O. Box 4404, N-0403 Oslo, (NO)
*RAFF, Howard"**, 296 Greene Street, Mill Valley, CA 94941, (US
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 1079857 A1 010307 (Basic)
WO 9961053 991202
APPLICATION (CC, No, Date): EP 99926046 990528; WO 99US11977 990528
PRIORITY (CC, No, Date): US 87351 980529; US 106446 981030
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/39; A61K-009/127; A61K-039/385
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
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Searcher : Shears 308-4994